National and Kapodistrian
UNIVERSITY OF ATHENS

Θεραπεία οξέος ισχαιμικού ΑΕΕ: Τί νεότερο?

Ελένη Κορομπόκη MD, PhD, FESO
Παθολόγος
Επιμελήτρια Α’ ΕΣΥ
Θεραπευτική Κλινική ΕΚΠΑ
Νοσοκομείο Αλεξάνδρα

Disclosures

- Funded Research: European Union's Horizon 2020 research and innovation programme under grant agreement No 754517.

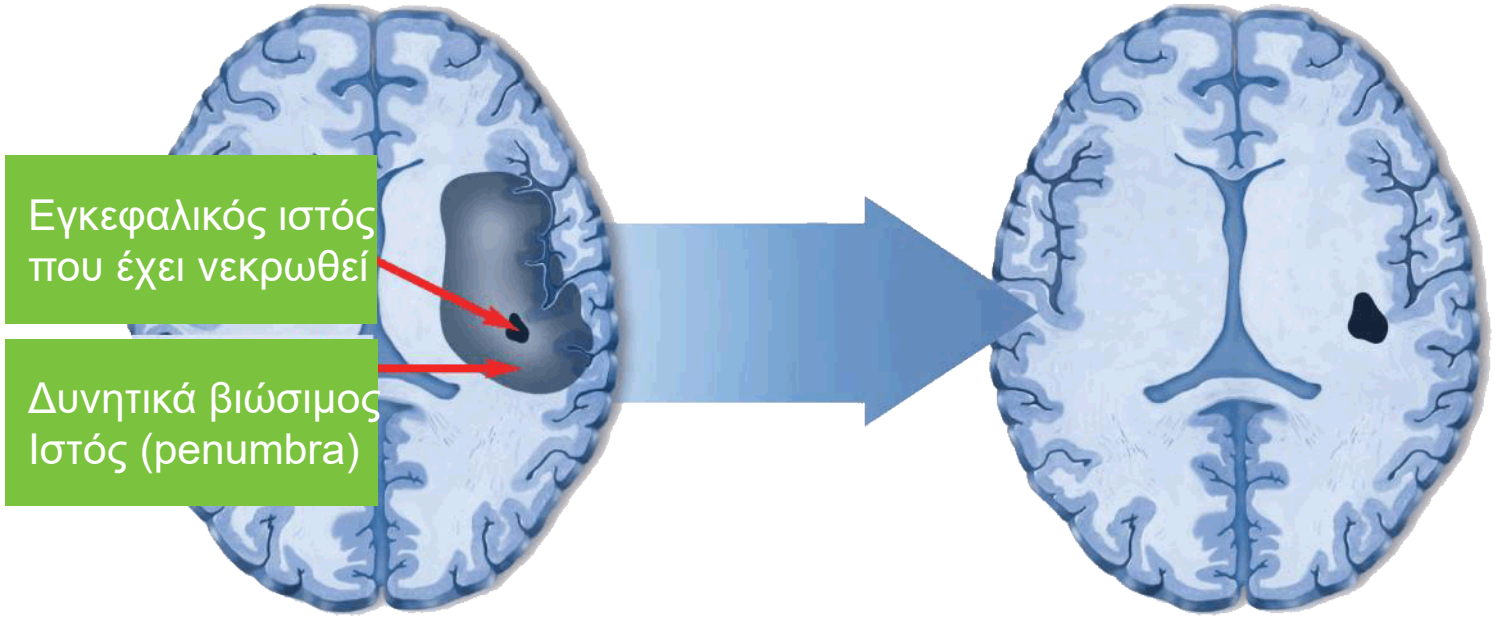
- Speaker Honoraria/Travel grants: Bayer, Pfizer, Amgen, ELPEN, INNOVIS, Sanofi

Το Αγγειακό Εγκεφαλικό Επεισόδιο αποτελεί υπερεπείγουσα κατάσταση και πρέπει να αντιμετωπίζεται ως οποιοδήποτε ιατρικό επείγον

Γιατί η θεραπεία στην οξεία φάση είναι σημαντική?

Κάθε λεπτό που περνά μετά από την εγκατάσταση του ΑΕΕ καταστρέφονται 1.9 εκατομμύρια νευρώνες, εάν ο ασθενής δε λάβει θεραπεία

Κάθε λεπτό που περνάει οδηγεί σε απώλεια εγκεφαλικού ιστού

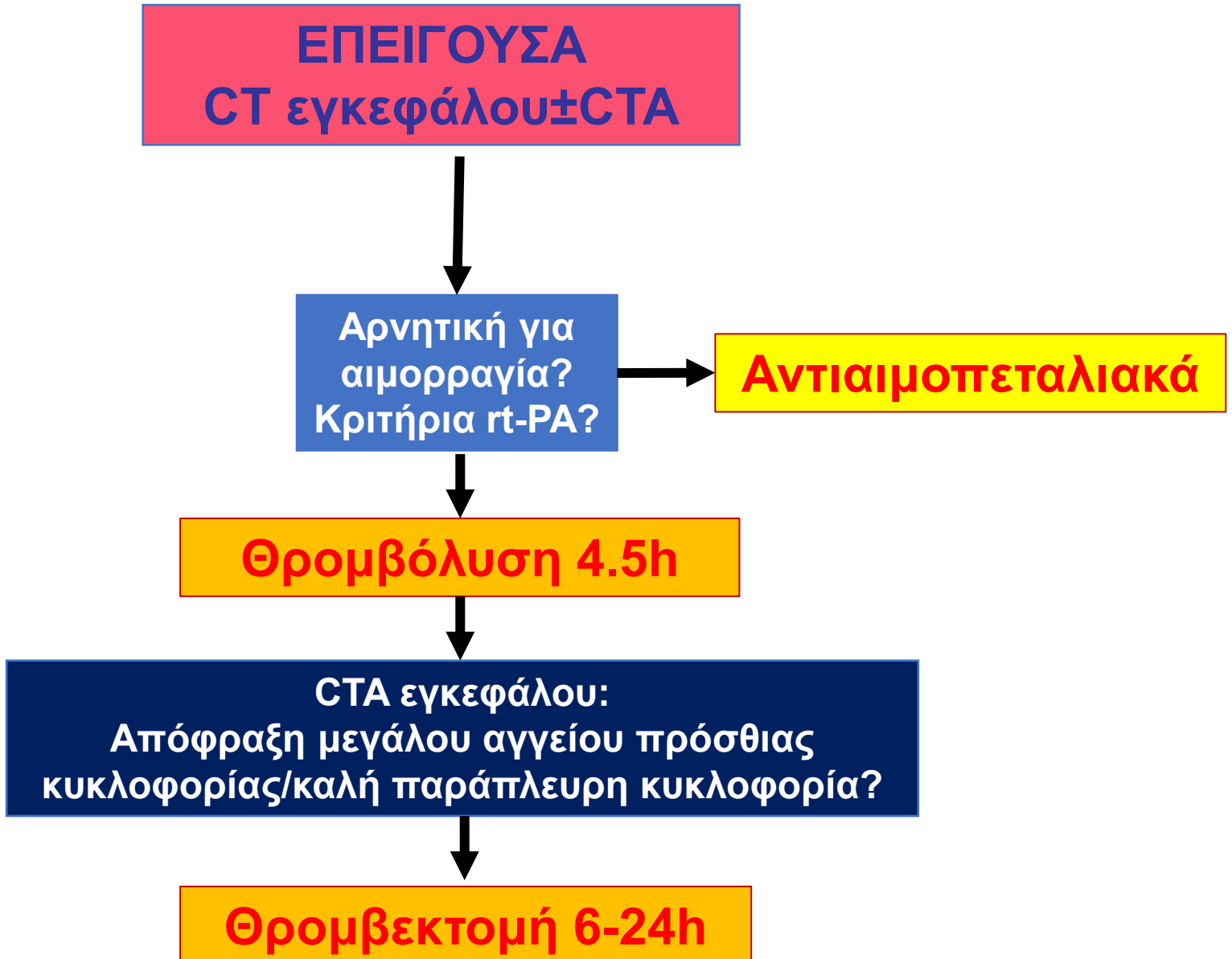


Κάθε λεπτό που περνάει μετά την έναρξη των συμπτωμάτων καταστρέφονται 1.9 εκατομμύρια νευρικά κύτταρα

Η θρομβόλυση και θρομβεκτομή βοηθούν στη επαναιμάτωση του εγκεφαλικού ιστού που δεν έχει ακόμα νεκρωθεί

Saver. Stroke 2006;37:263-266.
González. Am J Neuroradiol 2006;27:728-735.
Donnan. Lancet Neurol 2002;1:417-425.

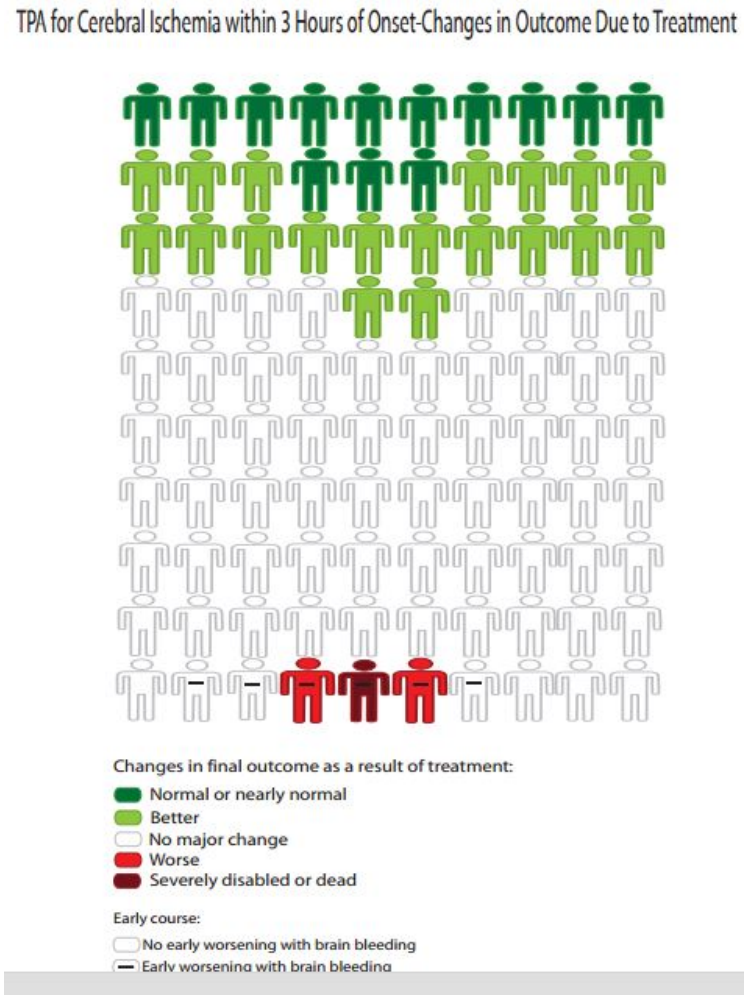
Επείγοντα -διαγνωστική προσπέλαση



Οι ελάχιστες προϋποθέσεις για τη θρομβόλυση

Εξακριβωμένη ώρα έναρξης συμπτωμάτων <4,5h	Ιατρικό ιστορικό, αποκλεισμός αντιπηκτικής αγωγής ή άλλης αντένδειξης	Νευρολογική εξέταση, βαθμός NIHSS	Γλυκόζη αίματος (η γλυκόζη αίματος είναι το μόνο απαραίτητο εργαστηριακό αποτέλεσμα που απαιτείται προ της έναρξης της θρομβόλυσης*)
Ζωτικά σημεία, ΑΠ<185/110mmHg	CT εγκεφάλου χωρίς σκιαγραφικό	Δύο φλεβικές γραμμές	Ξεκινούμε και συνεχίζουμε να ενοχλούμε τα εργαστήρια για τα αποτελέσματα των εργαστηριακών εξετάσεων (INR, PLT)

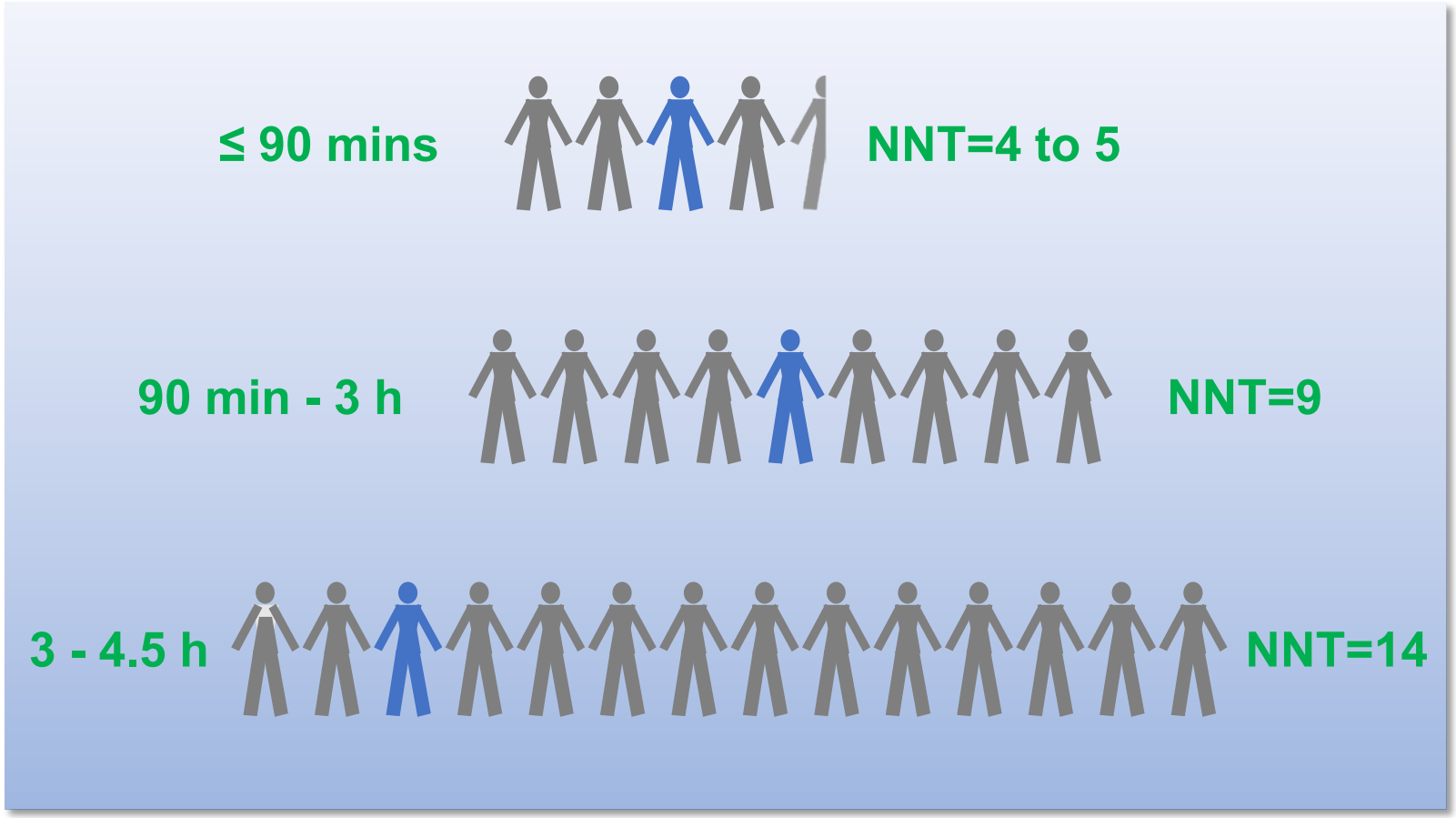
Αποτελεσματικότητα θρομβόλυσης τις 3 πρώτες ώρες



Ένας στους τέσσερις ασθενείς θα βελτιωθεί κλινικά (NNT=4)
Ένας στους οχτώ ασθενείς θα έχει μικρή αναπηρία ή θα είναι λειτουργικά ανεξάρτητος (NNT=8)

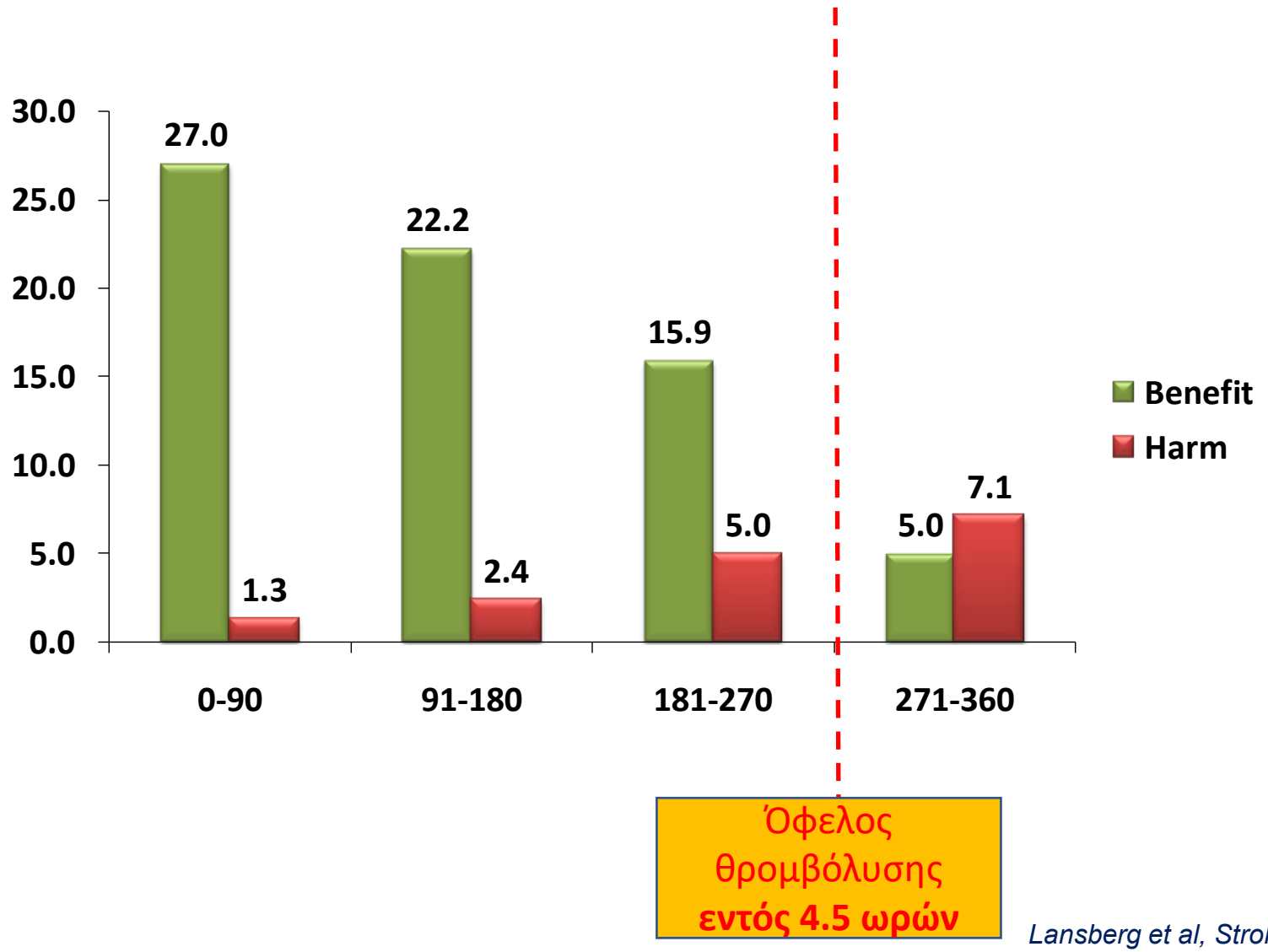
Saver et al. Arch Neurol. 2004;61:1066–1070

Η αποτελεσματικότητα της θρομβόλυσης είναι χρονοεξαρτώμενη



Lees et al. Lancet 2010;375:1695-1703.

Number of Patients Who Benefit and Are Harmed per 100 Patients tPA Treated in Each Time Window



Lansberg et al, Stroke 2009

Ενδοφλέβια θρομβόλυση

3.5. IV Alteplase

3.5. IV Alteplase	COR	LOE	New, Revised, or Unchanged
1. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is recommended for selected patients who may be treated within 3 hours of ischemic stroke symptom onset or patient last known well or at baseline state. Physicians should review the criteria outlined in Table 6 to determine patient eligibility.	I	A	Recommendation reworded for clarity from 2013 AIS Guidelines. Class and LOE unchanged. See Table LXXXIII in online Data Supplement 1 for original wording.
2. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 minutes with initial 10% of dose given as bolus over 1 minute) is also recommended for selected patients who can be treated within 3 and 4.5 hours of ischemic stroke symptom onset or patient last known well. Physicians should review the criteria outlined in Table 6 determine patient eligibility.	I	B-R	Recommendation reworded for clarity from 2013 AIS Guidelines. Class unchanged. LOE amended to conform with ACC/AHA 2015 Recommendation Classification System. See Table LXXXIII in online Data Supplement 1 for original wording.
13. In patients undergoing fibrinolytic therapy, physicians should be prepared to treat potential emergent adverse effects, including bleeding complications and angioedema that may cause partial airway obstruction.	I	B-NR	Recommendation reworded for clarity from 2013 AIS Guidelines. Class unchanged. LOE amended to conform with ACC/AHA 2015 Recommendation Classification System. See Table LXXXIII in online Data Supplement 1 for original wording.

AHA/ASA guidelines 2018

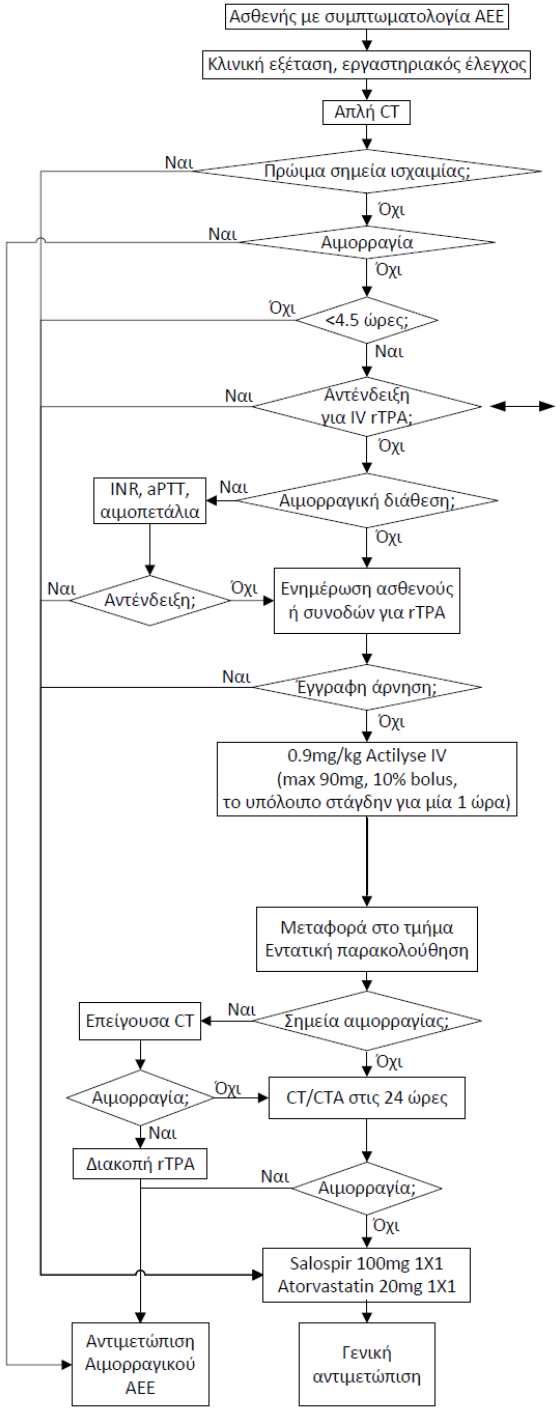
Δοσολογικό σχήμα Actilyse για iv θρομβόλυση σε ασθενείς με οξύ ισχαιμικό εγκεφαλικό

Η συνιστώμενη δόση Actilyse για ενδοφλέβια θρομβόλυση σε ασθενείς με οξύ εγκεφαλικό είναι **0.9 mg/kg (με μέγιστη δόση τα 90 mg)** η οποία πρέπει να εκχυθεί σε **60 minutes [με το 10% της συνολικής δόσης να εκχύεται ως δόση εφόδου (bolus) σε 1 λεπτό]**.

Βάρος (kg)	Συνολική δόση (mg ή ml)	Δόση εφόδου (mg ή ml)	Δόση στάγδην έκχυσης σε 60' (mg ή ml)
50	45	5	41
51	46	5	41
52	47	5	42
53	48	5	43
54	49	5	44
55	50	5	45
56	50	5	45
57	51	5	46
58	52	5	47
59	53	5	48
60	54	5	49
61	55	5	49
62	56	6	50
63	57	6	51
64	58	6	52
65	59	6	53
66	59	6	53
67	60	6	54
68	61	6	55
69	62	6	56
70	63	6	57
71	64	6	58
72	65	6	58
73	66	7	59
74	67	7	60
75	68	7	61
76	68	7	62
77	69	7	62
78	70	7	63
79	71	7	64
80	72	7	65
81	73	7	66
82	74	7	66
83	75	7	67
84	76	8	68
85	77	8	69
86	77	8	70
87	78	8	70
88	79	8	71
89	80	8	72
90	81	8	73
91	82	8	74
92	83	8	75
93	84	8	75
94	85	8	76
95	86	9	77
96	86	9	78
97	87	9	79
98	88	9	79
99	89	9	80
> 100	90	9	81

Recommendations: thrombolysis

- Intravenous rt-PA (0.9 mg/kg BW, maximum 90 mg), with 10% of the dose given as a bolus followed by a 60-minute infusion, is recommended **within 4.5 hours** of onset of ischemic stroke **(Class I, Level A)**



- >4.5 ώρες από την έναρξη του ΑΕΕ
- Ενδοκράνιος αιμορραγία (CT ή MRI)
- Υπόπυκνη περιοχή >30% της κατανομής της μέσης εγκεφαλικής αρτηρίας
- Άγνωστη ώρα έναρξης του ΑΕΕ
- NIHSS <4 ή >25
- Ραγδαία κλινική βελτίωση
- Ηλικία <18 ή >80*
- Πρόσφατο ΑΕΕ (<3 μήνες)
- Ιστορικό ΑΕΕ και συνύπαρξη ΣΔ
- Βαριά συννοσηρότητα
- Αιμορραγική διάθεση
- Βαριά ηπατοπάθεια
- Προηγούμενο αιμορραγικό ΑΕΕ
- Υποψία υπαραχνοειδούς αιμορραγίας
- ΑΠ >185/110 παρά τη χορήγηση IV ανθυπερτασικών
- Αιμοπετάλια <100,000/mm^3
- *Λήψη LMWH ή per os αντιπηκτικών (INR >1.5, aPTT >33sec)
- Υποψία ανευρύσματος αορτής
- Ένδο- ή περικαρδίτιδα, παγκρεατίτιδα
- Πρόσφατο (<3 μήνες) χειρουργείο/ αιμορραγία πεπτικού/ουροπ/κού
- *Σάκχαρο <50 ή >400mg/dl
- *Ενδοκράνιος όγκος ή ανεύρυσμα
- *Επιληπτική κρίση κατά το ΑΕΕ
- *Πρόσφατη (<10 ημ.) ανάνηψη/ παρακέντηση αρτηρίας/οσφυονωτιαία

Time is brain!

1.5. Hospital Stroke Teams	COR	LOE
1. An organized protocol for the emergency evaluation of patients with suspected stroke is recommended.	I	B-NR
2. It is recommended that DTN time goals be established. A primary goal of achieving DTN times within 60 minutes in ≥50% of AIS patients treated with IV alteplase should be established.	I	B-NR

Guideline

European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke

EUROPEAN STROKE JOURNAL

Recommendation

For patients with acute ischaemic stroke of <4.5 h duration, we recommend intravenous thrombolysis with alteplase.
Quality of evidence: **High** ⊕⊕⊕⊕
Strength of recommendation: **Strong** ↑↑

Recommendation

For patients with acute ischaemic stroke of <4.5 h duration, who are over 80 years of age, we recommend intravenous thrombolysis with alteplase.
Quality of evidence: **High** ⊕⊕⊕⊕
Strength of recommendation: **Strong** ↑↑

Η θρομβόλυση ενδείκνυται και στους ηλικιωμένους > 80 ετών

Berge et al., Eur Stroke J 2021

Θρομβόλυση σε ασθενείς με ιστορικό ΑΕΕ

Guideline

European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke

Expert consensus statement

For patients with acute ischaemic stroke of < 4.5 h duration, and a history of ischemic stroke within the last three months, nine of nine members voted for intravenous thrombolysis with alteplase in selected cases, for example in case of a small infarct, stroke occurring more than one month earlier, or good clinical recovery.

Expert consensus statement

For patients with acute ischaemic stroke of < 4.5 h duration and with a history of intracranial haemorrhage, 8 of 9 members suggest intravenous thrombolysis with alteplase in selected cases. For example, intravenous thrombolysis may be considered if a long time has elapsed since the haemorrhage, or if there was a non-recurrent or treated underlying cause for the haemorrhage (e.g. trauma, subarachnoid haemorrhage with subsequent endovascular or surgical aneurysm removal, or use of specific antithrombotic medication).

Ασθενείς με πρόσφατο ΑΕΕ εντός 3 μηνών θα μπορούσαν υπο προϋποθέσεις να λάβουν θρομβόλυση

Berge et al., Eur Stroke J 2021

Θρομβόλυση σε ασθενείς που λαμβάνουν αντιθρομβωτικά

Guideline

European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke

Recommendation

For patients with acute ischaemic stroke of < 4.5 h duration, who used single or dual antiplatelet agents prior to the stroke, we suggest intravenous thrombolysis with alteplase.
Quality of evidence: **Low** ⊕⊕
Strength of recommendation: **Strong** ↑↑

Recommendation

For patients with acute ischaemic stroke of < 4.5 h duration, who used a NOAC during the last 48 h before stroke onset, and for whom there is no specific coagulation tests available (i.e. calibrated anti-Xa-activity for factor Xa inhibitors, thrombin time for dabigatran, or the NOAC blood concentrations), we suggest no intravenous thrombolysis.
Quality of evidence: **Very Low** ⊕
Strength of recommendation: **Strong** ↓↓

Recommendation

For patients with acute ischaemic stroke of < 4.5 h duration, who use vitamin K antagonists and have INR ≤1.7 we recommend intravenous thrombolysis with alteplase.
Quality of evidence: **Low** ⊕⊕
Strength of recommendation: **Strong** ↑↑

For patients with acute ischaemic stroke of < 4.5 h duration, who use vitamin K antagonists and have INR >1.7 we recommend no intravenous thrombolysis.
Quality of evidence: **Very Low** ⊕
Strength of recommendation: **Strong** ↓↓

For patients with acute ischaemic stroke of < 4.5 h duration, who use vitamin K antagonists, and for whom the results of coagulation testing is unknown, we recommend no intravenous thrombolysis.
Quality of evidence: **Very low** ⊕
Strength of recommendation: **Strong** ↓↓

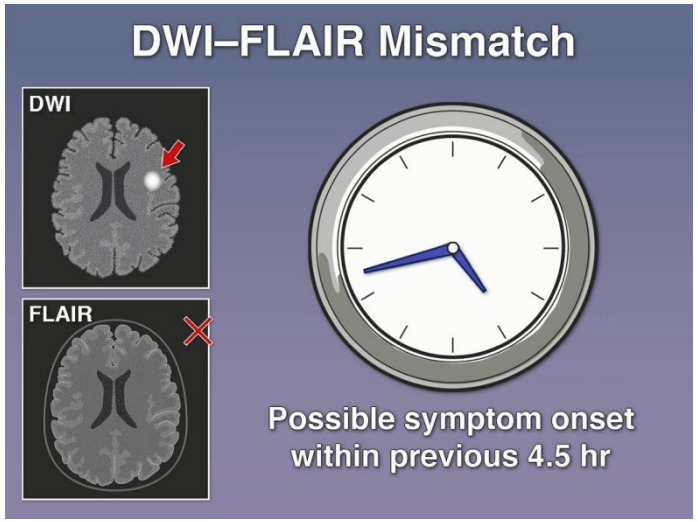
Berge et al., Eur Stroke J 2021

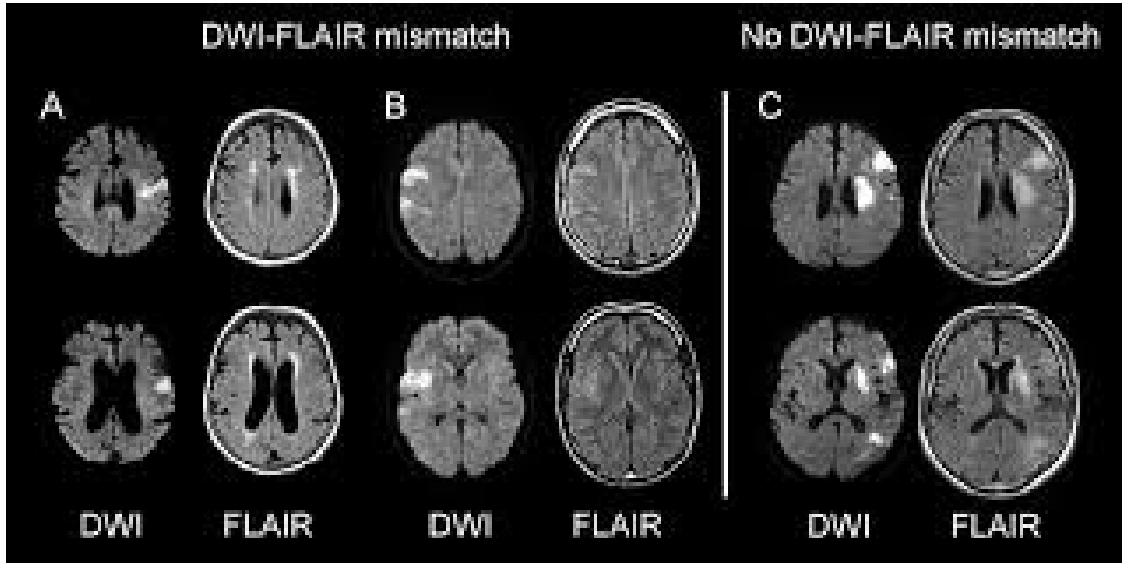
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 16, 2018 VOL. 379 NO. 7

MRI-Guided Thrombolysis for Stroke with Unknown Time of Onset

G. Thomalla, C.Z. Simonsen, F. Boutitie, G. Andersen, Y. Berthezene, B. Cheng, B. Cheripelli, T.-H. Cho, F. Fazekas, J. Fiehler, I. Ford, I. Galinovic, S. Gellissen, A. Golsari, J. Gregori, M. Günther, J. Guibernau, K.G. Häusler, M. Hennerici, A. Kemmling, J. Marstrand, B. Modrau, L. Neeb, N. Perez de la Ossa, J. Puig, P. Ringleb, P. Roy, E. Scheel, W. Schonewille, J. Serena, S. Sunaert, K. Villringer, A. Wouters, V. Thijs, M. Ebinger, M. Endres, J.B. Fiebach, R. Lemmens, K.W. Muir, N. Nighoghossian, S. Pedraza, and C. Gerloff, for the WAKE-UP Investigators*





WAKE-UP trial: αποτελεσματικότητα

Table 2. Primary and Secondary Efficacy Outcomes (Intention-to-Treat Population).*

Outcome	Alteplase Group (N=254)	Placebo Group (N=249)	Effect Variable	Adjusted Value (95% CI)†	P Value
Primary efficacy end point					
Favorable outcome at 90 days — no./total no. (%)‡	131/246 (53.3)	102/244 (41.8)	Odds ratio	1.61 (1.09 to 2.36)	0.02
Secondary efficacy end points					
Median score on modified Rankin scale at 90 days (IQR)§	1 (1–3)	2 (1–3)	Common odds ratio	1.62 (1.17 to 2.23)	0.003¶
Correlation between treatment response at 90 days and deficit level at baseline — no./total no. (%)‖	72/246 (29.3)	44/244 (18.0)	Odds ratio	1.88 (1.22 to 2.89)	0.004¶
Global Outcome Score at 90 days**			Odds ratio	1.47 (1.07 to 2.04)	0.02¶
Median score on Beck Depression Inventory at 90 days (IQR)††	6.0 (2.0–11.0)	7.0 (2.0–14.0)	Mean difference ($\log_e$)	−0.04 (−0.22 to 0.15)	0.69¶
Total score on EQ-5D at 90 days‡‡	1.9±2.1	2.4±2.4	Mean difference	−0.52 (−0.88 to −0.16)	0.004¶
Score on visual analog scale on EQ-5D at 90 days§§	72.6±19.7)	64.9±23.8	Mean difference	7.64 (3.75 to 11.51)	<0.001¶
Median infarct volume at 22–36 hr (IQR) — ml ¶¶	3.0 (0.8–17.7)	3.3 (1.1–16.6)	Mean difference ($\log_e$)	−0.16 (−0.47 to 0.15)	0.32¶

WAKE-UP trial: ασφάλεια

Table 3. Safety Outcomes.

Outcome	Alteplase Group (N=251)	Placebo Group (N=244)	Adjusted Odds Ratio (95% CI)*	P Value
	no. (%)			
Primary†				
Death or dependency at 90 days	33 (13.5)	44 (18.3)	0.68 (0.39–1.18)	0.17
Death at 90 days	10 (4.1)	3 (1.2)	3.38 (0.92–12.52)	0.07
Secondary				
Symptomatic intracranial hemorrhage				
As defined in SITS-MOST‡	5 (2.0)	1 (0.4)	4.95 (0.57–42.87)	0.15
As defined in ECASS II§	7 (2.8)	3 (1.2)	2.40 (0.60–9.53)	0.21
As defined in ECASS III¶	6 (2.4)	1 (0.4)	6.04 (0.72–50.87)	0.10
As defined in NINDS‖	20 (8.0)	12 (4.9)	1.78 (0.84–3.71)	0.13
Parenchymal hemorrhage type 2**	10 (4.0)	1 (0.4)	10.46 (1.32–82.77)	0.03
Other††				
Space-occupying brain infarction or edema with clinical deterioration	6 (2.4)	2 (0.8)		
Recurrent ischemic stroke				
Asymptomatic‡‡	58 (23.1)	55 (22.5)		
Symptomatic	17 (6.8)	8 (3.3)		
Major extracranial bleeding	3 (1.2)	0		
Severe anaphylactic reaction	0	1 (0.4)		

Περισσότερες αριθμητικά αιμορραγίες στο σκέλος της αλτεπλάσης

WAKE-UP trial: συμπεράσματα

- Η διενέργεια ενδοφλέβιας θρομβόλυσης με αλτεπλάση έναντι του placebo είναι αποτελεσματική σε επιλεγμένους ασθενείς με αγνώστου ενάρξεως ισχαιμικό εγκεφαλικό, βάσει των απεικονιστικών ευρημάτων σε ειδικές ακολουθίες της μαγνητικής τομογραφίας εγκεφάλου (MRI DWI/FLAIR).

- Δεν υπήρξε διαφορά στη θνητότητα

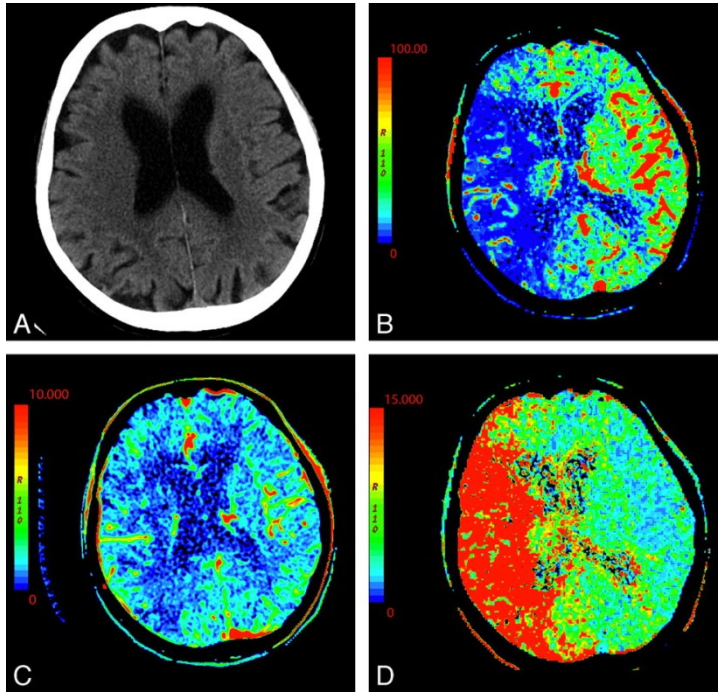
- Στο σκέλος της αλτεπλάσης παρατηρήθηκαν αριθμητικά περισσότερες αιμορραγίες

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 9, 2019 VOL. 380 NO. 19

Thrombolysis Guided by Perfusion Imaging up to 9 Hours after Onset of Stroke

H. Ma, B.C.V. Campbell, M.W. Parsons, L. Churilov, C.R. Levi, C. Hsu, T.J. Kleinig, T. Wijeratne, S. Curtze, H.M. Dewey, F. Miteff, C.-H. Tsai, J.-T. Lee, T.G. Phan, N. Mahant, M.-C. Sun, M. Krause, J. Sturm, R. Grimley, C.-H. Chen, C.-J. Hu, A.A. Wong, D. Field, Y. Sun, P.A. Barber, A. Sabet, J. Jannes, J.-S. Jeng, B. Clissold, R. Markus, C.-H. Lin, L.-M. Lien, C.F. Bladin, S. Christensen, N. Yassi, G. Sharma, A. Bivard, P.M. Desmond, B. Yan, P.J. Mitchell, V. Thijs, L. Carey, A. Meretoja, S.M. Davis, and G.A. Donnan, for the EXTEND Investigators*



EXTEND trial: Results

Table 2. Efficacy and Safety Outcomes.*

Outcome	Alteplase (N=113)	Placebo (N=112)	Adjusted Effect Size (95% CI)†	P Value	Unadjusted Effect Size (95% CI)†	P Value
	no./total no. (%)					
Primary outcome						
≥50%	76/106 (71.7)	57/109 (52.3)	1.35 (1.09–1.67)		1.37 (1.10–1.70)	
Tertiary outcomes						
Recanalization at 24 hr	72/107 (67.3)	43/109 (39.4%)	1.68 (1.29–2.19)		1.71 (1.30–2.23)	
Major neurologic improvement‖						
At 24 hr	27/113 (23.9)	11/112 (9.8)	2.76 (1.45–5.26)		2.43 (1.27–4.67)	
At 72 hr	32/112 (28.6)	22/112 (19.6)	1.56 (0.97–2.52)		1.45 (0.90–2.34)	
At 90 days	59/101 (58.4)	49/99 (49.5)	1.17 (0.91–1.52)		1.18 (0.91–1.53)	
Safety outcomes						
Death within 90 days after intervention	13/113 (11.5)	10/112 (8.9)	1.17 (0.57–2.40)	0.67	1.29 (0.59–2.82)	0.53
Symptomatic intracranial hemorrhage within 36 hr after intervention	7/113 (6.2)	1/112 (0.9)	7.22 (0.97–53.54)	0.053	6.94 (0.86–55.73)	0.07

Αποτελεσματική η θρομβόλυση μεταξύ 4.5-9 ωρών σε επιλεγμένους ασθενείς βάσει απεικονιστικών ευρημάτων (CT/MRI perfusion/diffusion)

Αριθμητικά περισσότερες αιμορραγίες

European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke

Recommendation

For patients with acute ischaemic stroke on awakening from sleep, who were last seen well more than 4.5 h earlier, who have MRI DWI-FLAIR mismatch, and for whom mechanical thrombectomy is either not indicated or not planned, we recommend intravenous thrombolysis with alteplase.
Quality of evidence: **High** ⊕⊕⊕⊕
Strength of recommendation: **Strong** ↑↑

For patients with acute ischaemic stroke on awakening from sleep, who have CT or MRI core/perfusion mismatch* within 9 h from the midpoint of sleep, and for whom mechanical thrombectomy is either not indicated or not planned, we recommend intravenous thrombolysis with alteplase.
Quality of evidence: **Moderate** ⊕⊕⊕
Strength of recommendation: **Strong** ↑↑

Expert consensus statement

For patients presenting directly to a thrombectomy centre with acute ischaemic stroke on awakening from sleep, who would be eligible for both IVT and mechanical thrombectomy, 6 of 9 group members suggest IVT before MT.

For patients presenting to a non-thrombectomy centre with acute ischaemic stroke on awakening from sleep, who would be eligible for both IVT and mechanical thrombectomy, 7 of 9 group members suggest IVT before MT.

Επέκταση του παραθύρου της θρομβόλυσης σε ΕΠΙΛΕΓΜΕΝΟΥΣ ασθενείς με βάση απεικονιστικά κριτήρια

Γιατί οι ασθενείς με βαρύ ισχαιμικό Εγκεφαλικό δεν ανταποκρίνονται καλά στην θρομβολυτική αγωγή ?

Real-World Experience and a Call for Action

- 127 patients with iv thrombolysis underwent furth
  assess recanalization (angio)
- **Only 21.25% patients had ac**
  - Distal ICA (4.4%)
  - M1-MCA 21 of 65
  - M2-MCA 4 of
  - Basilar

Άλλο θρομβολυτικό φάρμακο?
Επεμβατικές τεχνικές?

Bhatia R et al. Stroke 2010;41:2254-2258

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 26, 2018 VOL. 378 NO. 17

Tenecteplase versus Alteplase before Thrombectomy for Ischemic Stroke

B.C.V. Campbell, P.J. Mitchell, L. Churilov, N. Yassi, T.J. Kleinig, R.J. Dowling, B. Yan, S.J. Bush, H.M. Dewey, V. Thijs, R. Scroop, M. Simpson, M. Brooks, H. Asadi, T.Y. Wu, D.G. Shah, T. Wijeratne, T. Ang, F. Miteff, C.R. Levi, E. Rodrigues, H. Zhao, P. Salvaris, C. Garcia-Esperon, P. Bailey, H. Rice, L. de Villiers, H. Brown, K. Redmond, D. Leggett, J.N. Fink, W. Collecutt, A.A. Wong, C. Muller, A. Coulthard, K. Mitchell, J. Clouston, K. Mahady, D. Field, H. Ma, T.G. Phan, W. Chong, R.V. Chandra, L.-A. Slater, M. Krause, T.J. Harrington, K.C. Faulder, B.S. Steinfort, C.F. Bladin, G. Sharma, P.M. Desmond, M.W. Parsons, G.A. Donnan, and S.M. Davis, for the EXTEND-IA TNK Investigators*

Tenecteplase: the future of thrombolysis?

TNK vs. alteplase

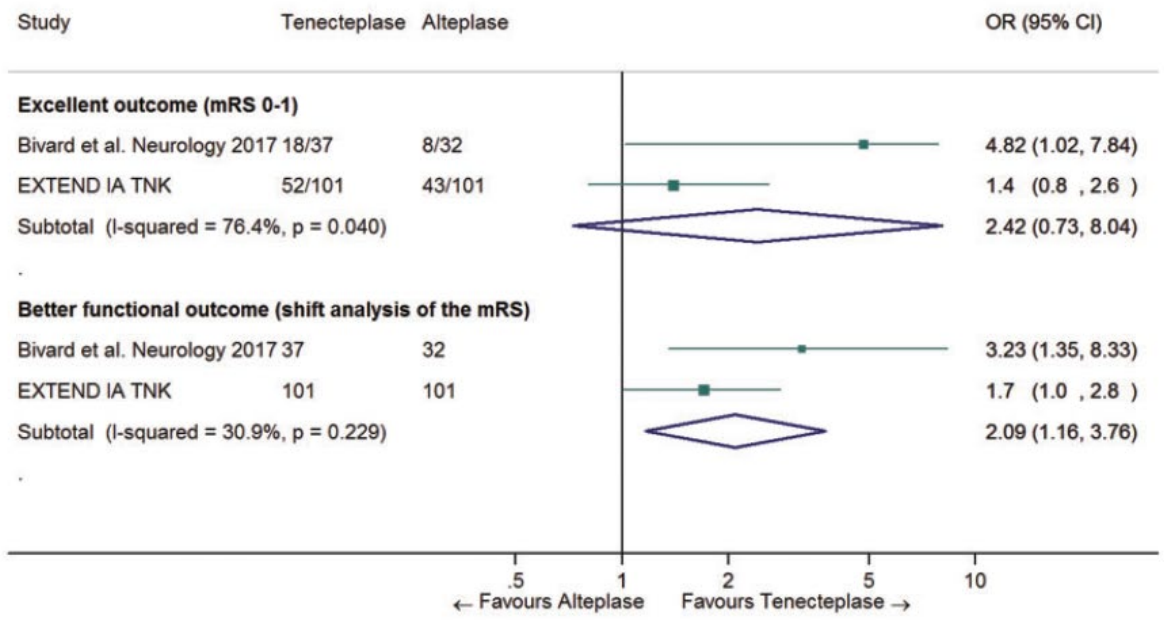
	Fibrin Selectivity	PAI-1 Resistance	Half-Life Time	Platelet-Rich Thrombus Activity	BBB Damage	Fibrinogen Depletion	HDL-C Level Lowering	Thrombolytic Potency
Alteplase	Moderate	Low	4–8min	Low	Moderate	Moderate	Moderate	Low
TNK	High	Moderate	11–20min	High	Unknown	Low	Low	High

Higher fibrin affinity
Longer half-life
Single IV bolus injection

Clinical trials on TNK in acute IS

Name Year	EXTEND IA TNK II[18] 2020	EXTEND IA TNK[17] 2018	NOR-TEST[16] 2017	ATTEST[15] 2015	TAAIS[13] 2012	Haley et al[12] 2010
Study design	PROBE	PROBE	PROBE	PROBE	PROBE	Multi-center, perspective randomized controlled trial
Dose	0.4 mg/kg 0.25 mg/kg	0.25 mg/kg	0.4 mg/kg	0.25 mg/kg	0.1 mg/kg 0.25 mg/kg	0.1 mg/kg 0.25 mg/kg 0.4 mg/kg
Time window	4.5h	4.5h	4.5h	4.5h	6h	3h
Imaging	ICA/MCA/BA occlusion	ICA/MCA/BA occlusion			CTA: intracranial vessel occlusion; CTP: TTP≥core volume 20%, core volume≤20mL	
Sample size	300	202	1100	96	75	112
Initial NIHSS	16 VS 17	17 VS 17	5.6 VS 5.8	12 VS 11	14.5 VS 14.6 VS 14	8 VS 10 VS 9 VS 13
90d mRS 0–1	49 VS 49%(p=0.69)	51 VS 43%(p=0.20)	64% VS 63% (p=0.52)	28% VS 20% (p=0.28)	54% VS 40%(p=0.25)	45.2% VS 48.4% VS 36.8% VS 41.9%
Symptomatic intracranial hemorrhage	PH2 36h: 1.3VS. 4.7% (p=0.12)	PH2 36h: 1 VS 1% (p=0.99)	ECASS III: 3 VS 2% (p=0.70)	ECASS III: 6% VS 8% (p=0.59) SITS-MOST: 2% VS 4% (p=0.50)	SITS-MOST: 4 VS 12% (p=0.33)	0% VS 6.5% VS 15.8% VS 3.2%
Mortality	15 VS 17% (p=0.35)	10 VS 18% (p=0.049)	5 VS 5% (p=0.68)	17% VS 12% (p=0.51)	8 VS 12% (p=0.68)	6.5% VS 22.6% VS 15.8% VS 25.8%

European Stroke Organisation (ESO) guidelines on intravenous thrombolysis for acute ischaemic stroke

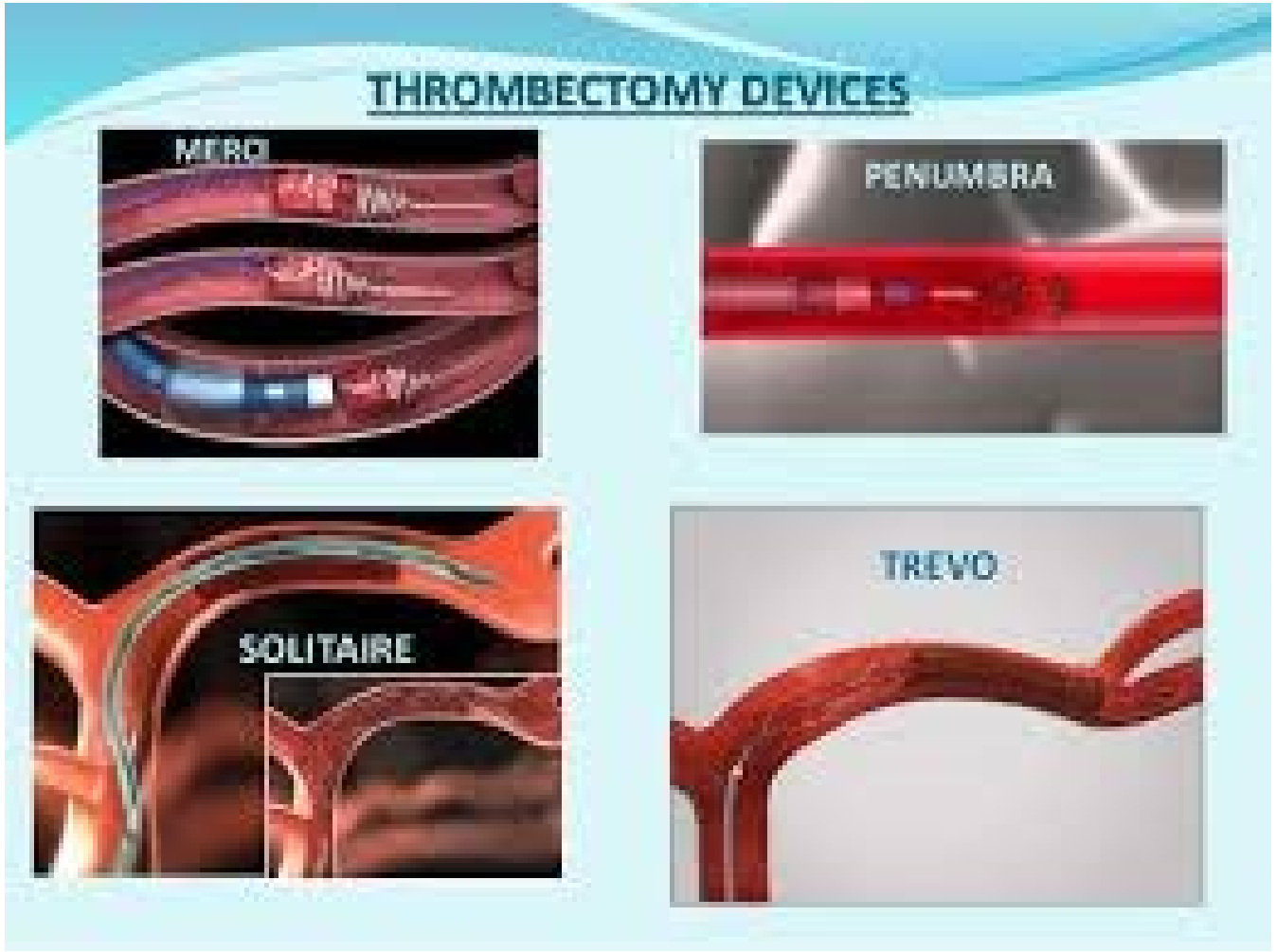


Recommendation

For patients with acute ischaemic stroke of < 4.5 h duration and with large vessel occlusion who are candidates for mechanical thrombectomy and for whom intravenous thrombolysis is considered before thrombectomy, we suggest intravenous thrombolysis with tenecteplase 0.25 mg/kg over intravenous thrombolysis with alteplase 0.9 mg/kg.
Quality of evidence: **Low** ⊕⊕
Strength of recommendation: **Weak** ↑?

Η θρομβόλυση με τενεκτεπλάση προκρίνεται στους ασθενείς που είναι υποψήφιοι για θρομβεκτομή

Θρομβεκτομή



JACC: CARDIOVASCULAR INTERVENTIONS
VOL. ■, NO. ■, 2016

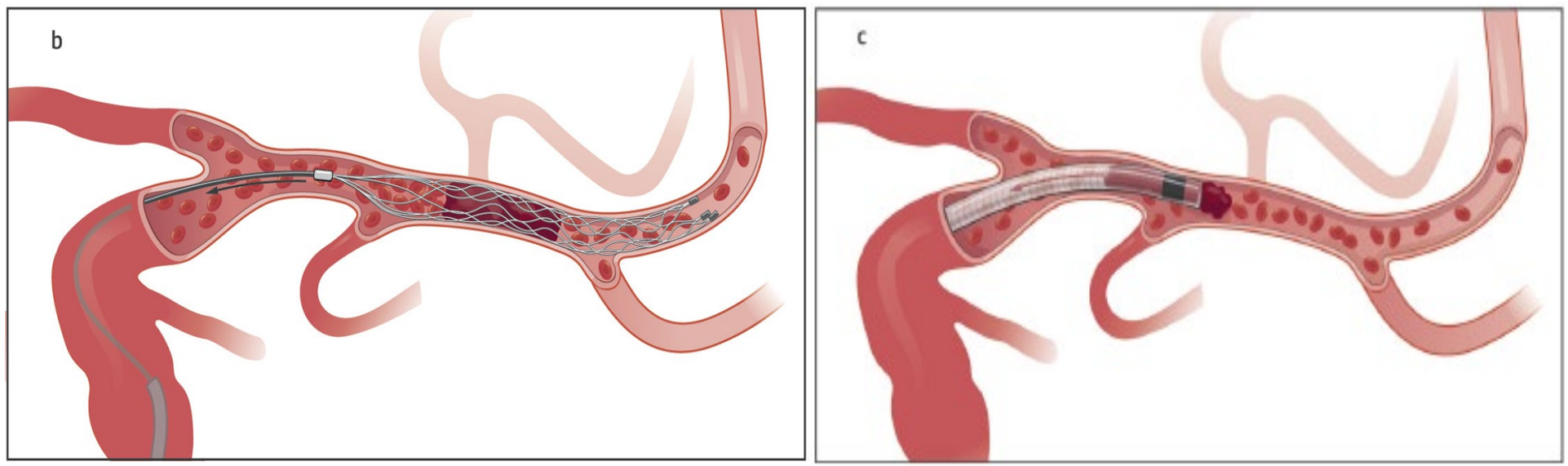
ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcin.2015.11.014

Endovascular Reperfusion Strategies for Acute Stroke

Panagiotis Papanagiotou, MD, PhD,[a,b] Christopher J. White, MD, MSCAI[c]

Stent retriever technique

Aspiration technique



Τυχαιοποιημένες μελέτες Μηχανικής Θρομβεκτομής με ή χωρίς θρομβόλυση έναντι IV Θρομβόλυσης

Μελέτη	MR-CLEAN	ESCAPE	EXTEND-IA	SWIFT-PRIME	REVASCAT
Ασθενείς (n)	500	315	70	195	206
Θρομβεκτομή± θρομβόλυση vs θρομβόλυση	233 / 267	165 / 150	35 / 35	98 / 97	103 / 103
Χρόνος θεραπείας	<6 ώρες	<12 ώρες	<4.5 ώρες	<6 ώρες	<8 ώρες
***mRS 0-2 (%)**	32.6 / 19.1 **OR 2.16** (95%CI, 1.4-3.4)	53.0 / 29.3 **OR 2.6** (95%CI, 1.7-3.8)	71.0 / 40.0 **OR 4.2** (95%CI, 1.4-12.0)	60.2 / 35.5 **OR 2.75** (95%CI, 1.5-5.0)	43.7 / 28.2 **OR 2.1** (95% CI, 1.1-4.0)
Θνητότητα	9.0 / 8.2 ns	10.4 / 19.0 OR 0.5 (95%CI, 0.3-1.0)	9.0 / 20.0 OR 0.38 (95%CI, 0.1-1.6)	9.2 / 12.4 OR 0.72 (95%CI, 0.3-2.8)	18.4 / 15.5 OR 1.2 (95%CI, 0.6 to 2.2)
Εγκεφαλική αιμορραγία	ns	3.6 / 2.7 ns	0 / 6 ns	9.2 / 8.2 ns	1.9 / 1.9 ns

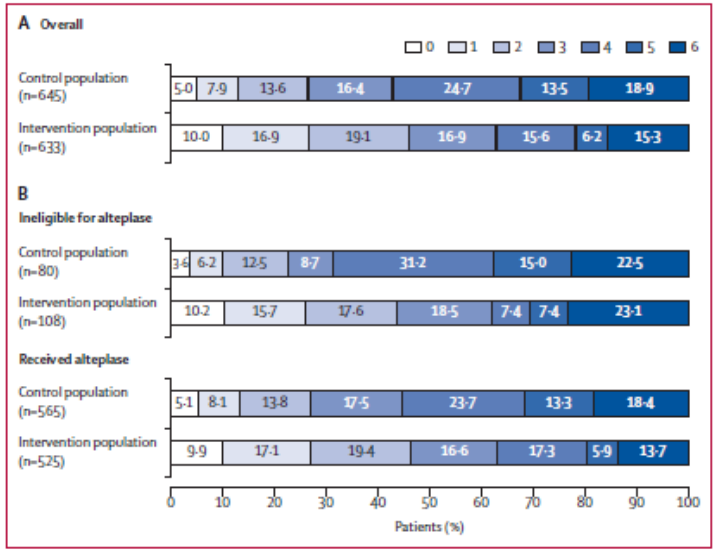
mRS 0-2: καθόλου ή ελαφρά αναπηρία.
Έκβαση: 90 ημέρες

N Engl J Med. 2015 Jan 1;372:11-20,
N Engl J Med. 2015 Mar 12;372:1019-30,
N Engl J Med. 2015 Mar 12;372:1009-18,
N Engl J Med. 2015 Jun 11;372:2285-95,
N Engl J Med. 2015 Jun 11;372(24):2296-306.

Endovascular Thrombectomy trials

Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials

MR CLEAN
ESCAPE
REVASCAT
SWIFT PRIME
EXTEND




Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials

Mayank Goyal, Bijoy K Menon, Wim H van Zwam, Diederik W J Dippel, Peter J Mitchell, Andrew M Demchuk, Antoni Dávalos, Charles B L M Majoie, Aad van der Lugt, Maria A de Miquel, Geoffrey A Donnan, Yvo B W E M Roos, Alain Bonafé, Reza Jahan, Hans-Christoph Diener, Lucie A van den Berg, Elad I Levy, Olvert A Berkhemer, Vitor M Pereira, Jeremy Rempel, Mónica Millán, Stephen M Davis, Daniel Roy, John Thornton, Luis San Román, Marc Ribó, Debbie Beumer, Bruce Stouch, Scott Brown, Bruce C V Campbell, Robert J van Oostenbrugge, Jeffrey L Saver, Michael D Hill, Tudor G Jovin, for the HERMES collaborators

Summary

Background In 2015, five randomised trials showed efficacy of endovascular thrombectomy over standard medical care in patients with acute ischaemic stroke caused by occlusion of arteries of the proximal anterior circulation. In this meta-analysis we, the trial investigators, aimed to pool individual patient data from these trials to address remaining questions about whether the therapy is efficacious across the diverse populations included.

Methods We formed the HERMES collaboration to pool patient-level data from five trials (MR CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, and EXTEND IA) done between December, 2010, and December, 2014. In these trials, patients with acute ischaemic stroke caused by occlusion of the proximal anterior artery circulation were randomly assigned to receive either endovascular thrombectomy within 12 h of symptom onset or standard care (control), with a primary outcome of reduced disability on the modified Rankin Scale (mRS) at 90 days. By direct access to the study databases, we extracted individual patient data that we used to assess the primary outcome of reduced disability on mRS at 90 days in the pooled population and examine heterogeneity of this treatment effect across prespecified subgroups. To account for between-trial variance we used mixed-effects modelling with random effects for parameters of interest. We then used mixed-effects ordinal logistic regression models to calculate common odds ratios (cOR) for the primary outcome in the whole population (shift analysis) and in subgroups after adjustment for age, sex, baseline stroke severity (National Institutes of Health Stroke Scale score), site of occlusion (internal carotid artery vs M1 segment of middle cerebral artery vs M2 segment of middle cerebral artery), intravenous alteplase (yes vs no), baseline Alberta Stroke Program Early CT score, and time from stroke onset to randomisation.

Findings We analysed individual data for 1287 patients (634 assigned to endovascular thrombectomy, 653 assigned to control). Endovascular thrombectomy led to significantly reduced disability at 90 days compared with control (adjusted cOR 2·49, 95% CI 1·76–3·53; p<0·0001). The number needed to treat with endovascular thrombectomy to reduce disability by at least one level on mRS for one patient was 2·6. Subgroup analysis of the primary endpoint showed no heterogeneity of treatment effect across prespecified subgroups for reduced disability ($p_{heterogeneity}$=0·43). Effect sizes favouring endovascular thrombectomy over control were present in several strata of special interest, including in patients aged 80 years or older (cOR 3·68, 95% CI 1·95–6·92), those randomised more than 300 min after symptom onset (1·76, 1·05–2·97), and those not eligible for intravenous alteplase (2·43, 1·30–4·55). Mortality at 90 days and risk of parenchymal haematoma and symptomatic intracranial haemorrhage did not differ between populations.

Interpretation Endovascular thrombectomy is of benefit to most patients with acute ischaemic stroke caused by occlusion of the proximal anterior circulation, irrespective of patient characteristics or geographical location. These findings will have global implications on structuring systems of care to provide timely treatment to patients with acute ischaemic stroke due to large vessel occlusion.

Funding Medtronic.

Introduction

Endovascular thrombectomy for acute ischaemic stroke has evolved substantially; however, only after the 2015 publication of five clinical trials[1–5] has this procedure been accepted as the standard of care for patients with proximal anterior circulation occlusions.[6] Uncertainties remain about the benefit of endovascular thrombectomy in patient groups under-represented in these individual trials, including those who presented to treatment late, are elderly, have mild deficits, and are not eligible for intravenous alteplase.[6] Moreover, because these trials were individually moderate in size, data pooling can provide more precise estimates of treatment effects. As investigators from the MR CLEAN, ESCAPE, SWIFT PRIME, REVASCAT, and EXTEND IA trials, we seek to address these and other questions about the risks and

Goyal et al., Lancet 2016

Thrombectomy trials baseline characteristics

	Intervention population (n=634)	Control population (n=653)
Demographic characteristics		
Median age (years)	68 (57-77)	68 (59-76)*
Men	330 (52%)	352 (54%)
Women	304 (48%)	301 (46%)
Past medical history		
Hypertension	352 (56%)	388 (59%)
Diabetes mellitus	82 (13%)	88 (13%)
Atrial fibrillation	209 (33%)	215 (33%)
Smoking (recent or current)	194 (31%)	210 (32%)
Clinical characteristics		
Baseline NIHSS score	17 (14-20)†	17 (13-21)‡
Baseline blood glucose (mmol/L)	6·6 (5·9-7·8)§	6·7 (5·9-7·8)¶
Imaging characteristics		
ASPECTS on baseline CT	9 (7-10)§	9 (8-10)¶
Intracranial occlusion location		
Internal carotid artery	133 (21%)	144 (22%)
M1 segment middle cerebral artery	439 (69%)	452 (69%)
M2 segment middle cerebral artery	51 (8%)	44 (7%)
Other	11 (2%)	13 (2%)
Treatment details and process times		
Treatment with intravenous alteplase	526 (83%)	569 (87%)
Treatment with intravenous alteplase documented within 180 min	442 (70%)	462 (71%)
Process times (min)		
Onset to randomisation	195·5 (142-260)‖	196 (142-270)*
Onset to intravenous alteplase	100 (75-133)**	100 (74-140)††
Onset to reperfusion	285 (210-362)	NA

Data are median (IQR), n (%), or mean (SD). NIHSS=National Institutes of Health Stroke Scale. ASPECTS=Alberta Stroke Program Early CT Score. *n=650. †n=631. ‡n=648. §n=620. ¶n=644. ‖n=632. **n=598. ††n=618.

Table 1: **Baseline characteristics in the pooled data**

Goyal et al., Lancet 2016

Thrombectomy RCTs meta-analysis

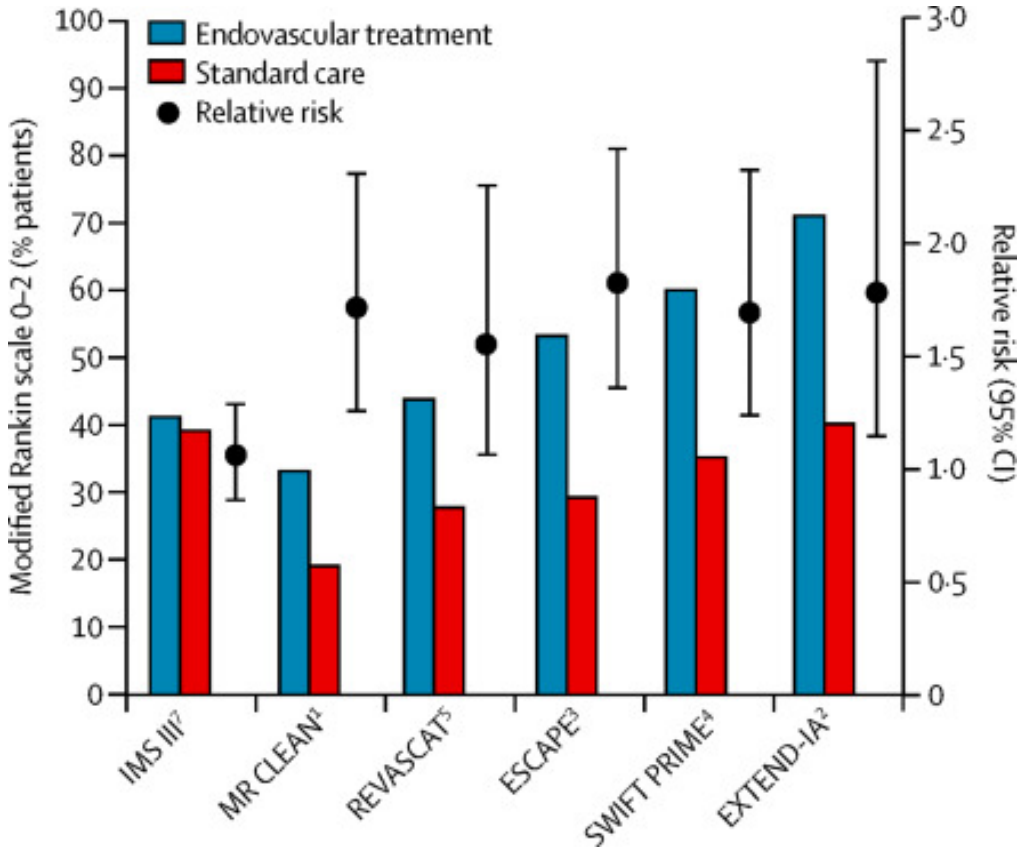
	Intervention population	Control population	Risk difference (%)	Rate ratio (95% CI)	Odds ratio (95% CI)	Adjusted rate ratio (95% CI)	Adjusted odds ratio (95% CI)
mRS score reduction (shift analysis; primary outcome)*	..	..	..	..	2·26* (1·67–3·06); p<0·0001	..	2·49* (1·76–3·53); p<0·0001
mRS score 0–1 at 90 days	26·9% (170/633)	12·9% (83/645)	14·0	2·00 (1·54–2·60); p<0·0001	2·49 (1·84–3·35); p<0·0001	2·06 (1·59–2·69); p<0·0001	2·72 (1·99–3·71); p<0·0001
mRS score 0–2 at 90 days	46·0% (291/633)	26·5% (171/645)	19·5	1·7 (1·41–2·05); p<0·0001	2·35 (1·85–2·98); p<0·0001	1·73 (1·43–2·09); p<0·0001	2·71 (2·07–3·55); p<0·0001
NIHSS score 0–2 at 24 h	21·0% (129/615)	8·3% (52/630)	12·7	2·47 (1·79–3·41); p<0·0001	2·91 (2·06–4·12); p<0·0001	2·66 (1·92–3·67); p<0·0001	3·77 (2·49–5·71); p<0·0001
Early neurological recovery at 24 h	50·2% (309/616)	21·2% (134/633)	29·0	2·34 (1·91–2·87); p<0·0001	4·04 (2·75–5·93); p<0·0001	2·34 (1·91–2·87); p<0·0001	4·36 (3·03–6·27); p<0·0001

Data show the proportion of patients with outcome (n/N), unless otherwise stated. NIHSS=National Institutes of Health Stroke Scale. mRS=modified Rankin Scale. *Common odds ratio indicating the odds of improvement of 1 point on the mRS.

Table 2: Efficacy outcomes from the pooled data

Goyal et al., Lancet 2016

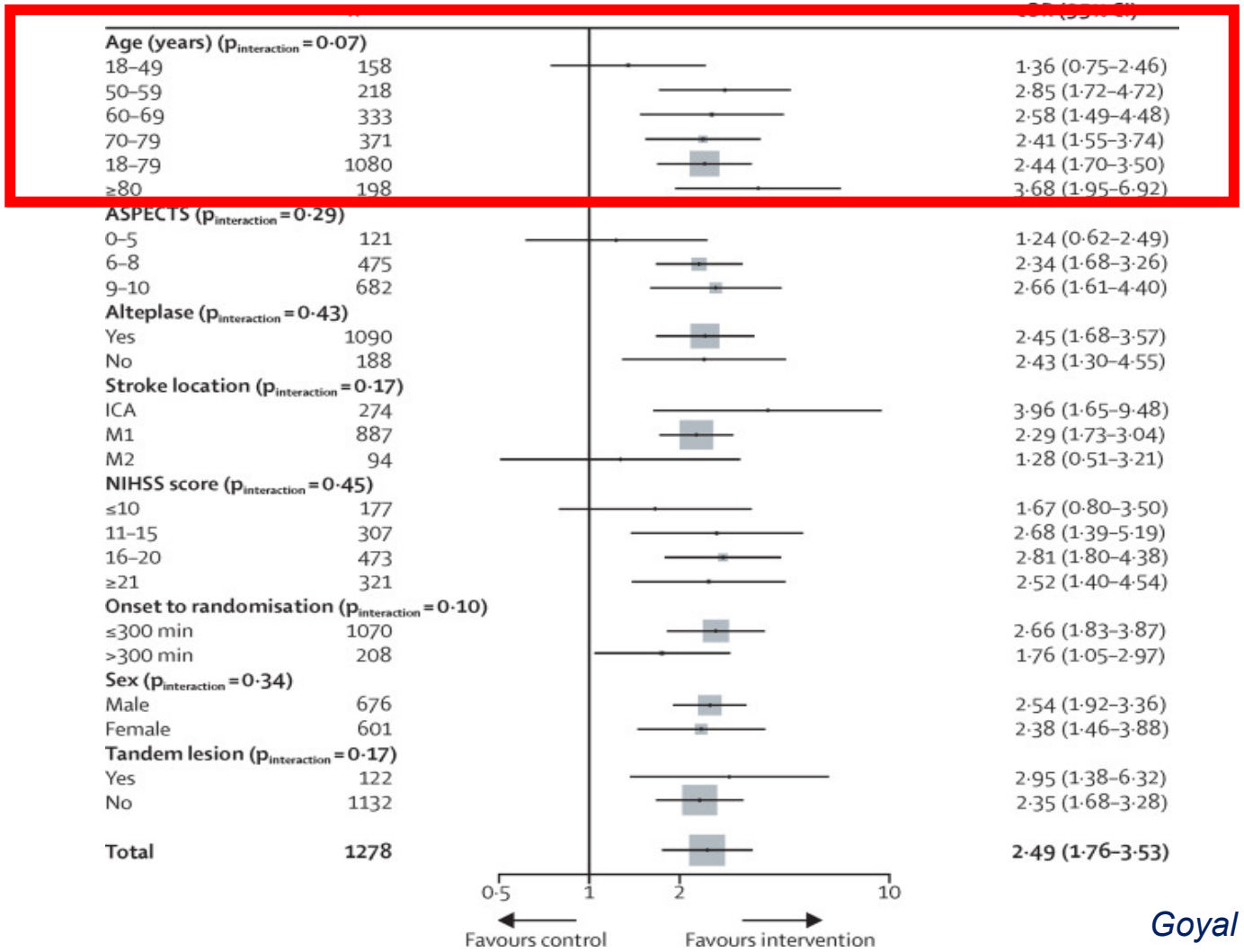
Thrombectomy RCTs



Endovascular thrombectomy is of benefit to most patients with acute IS caused by occlusion of the proximal anterior circulation, irrespective of patients characteristics or geographical location

Goyal et al., Lancet 2016

Subgroup analysis *(HERMES)*



Goyal M, et al. Lancet. 2016;387:1723-31

Acute Stroke interventions: evidence base

Intervention	Outcome	RRR	ARR	NNT
All stroke types and severities				
Stroke Unit care Cochrane 2007	Death/Dependency	17	3.6	28
Ischemic Stroke				
tPA <4.5hr Emberson et al, 2014	mRS 0-1	20	6.8	15
thombectomy <6hr MR-CLEAN ,EXTEND-IA, ESCAPE, SWIFT-PRIME, 2015	Death/Dependency	70	30	3
Aspirin IST, CAST 1997	Recurrent stroke/Death	10	0.9	111

AHA/ASA Guideline

2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

ΑΕΕ πρόσθιας κυκλοφορίας, απόφραξη μεγάλου κλάδου (ICA, MCA)

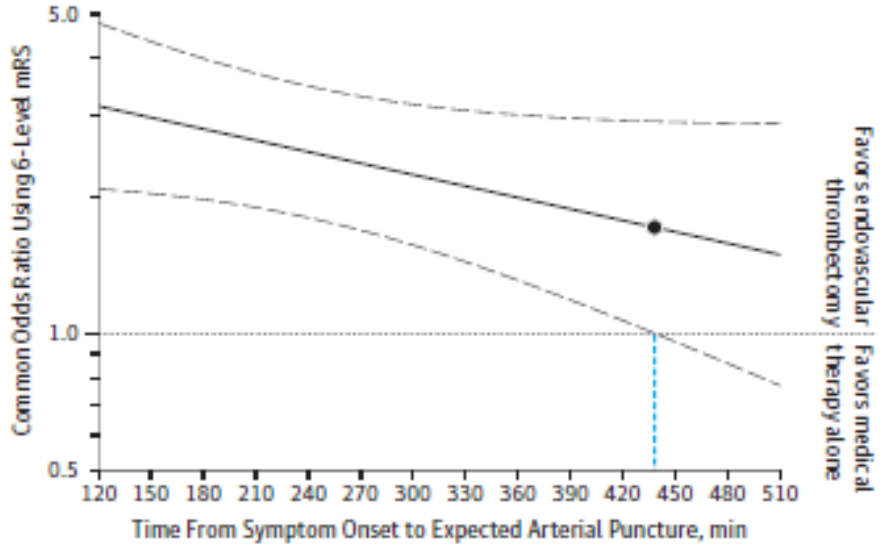
3.7. Mechanical Thrombectomy	COR	LOE
1. Patients eligible for IV alteplase should receive IV alteplase even if EVTs are being considered.	I	A
3. Patients should receive mechanical thrombectomy with a stent retriever if they meet all the following criteria: (1) prestroke mRS score of 0 to 1; (2) causative occlusion of the internal carotid artery or MCA segment 1 (M1); (3) age ≥18 years; (4) NIHSS score of ≥6; (5) ASPECTS of ≥6; and (6) treatment can be initiated (groin puncture) within 6 hours of symptom onset.	I	A

CT/CTA

AHA/ASA guidelines 2018

Time window and stroke outcome

- Benefits from thrombectomy rapidly decays over time and may no longer exist beyond 7.3 hours from stroke onset

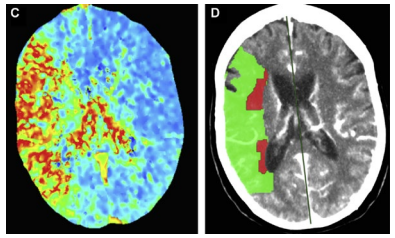


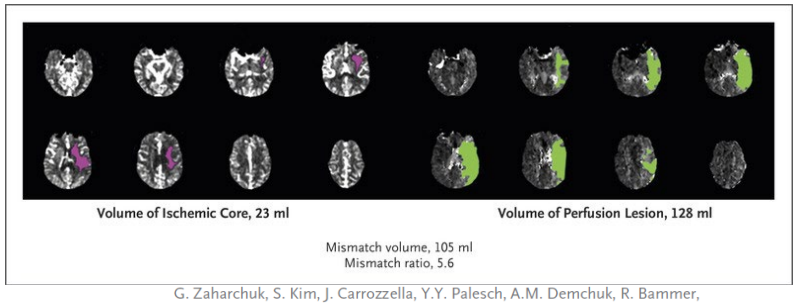
Time window for thrombectomy in selected patients:
6 hours

Saver at al. JAMA 2016

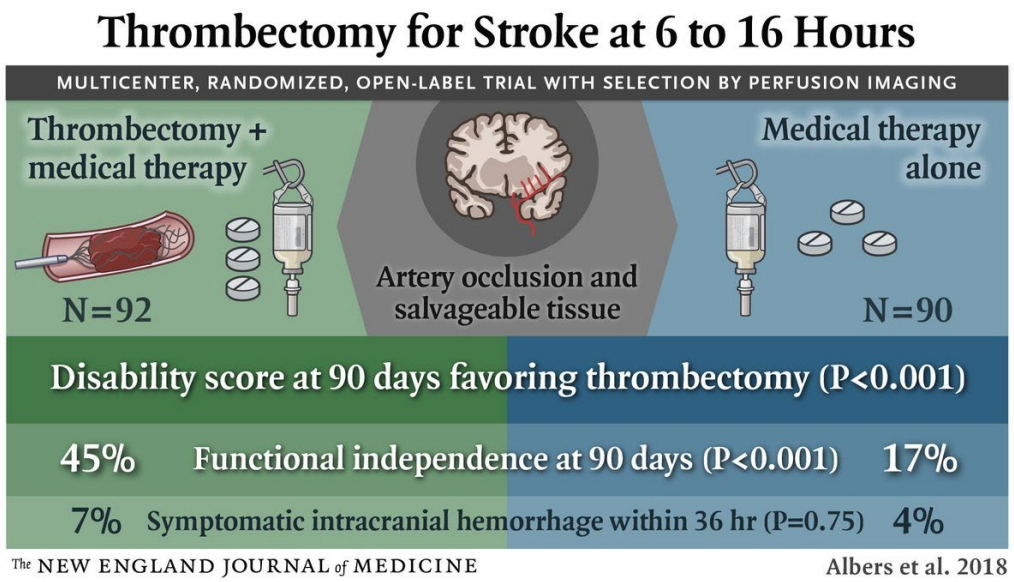
	SWIFT PRIME (Global)	EXTEND IA (AUS, NZ)	REVASCAT (Spain)	ESCAPE (Global)	MR CLEAN (Netherlands)
Randomization of patients to best medical care vs best medical care + Endovascular	✓	✓	✓	✓	✓
Time Window Studied	Onset to 6 hours	Onset to 6 hours	Onset to 8 hours	Onset to 12 hours	Onset to 6 hours
Number of Patients	196	70	206	316	500
Age	18-80	>18	18-80	>18	>18
Analysis of Primary Endpoint	Rankin Shift	Reperfusion at 24 hrs and dramatic NIHSS improvement at 3d	Rankin Shift	Rankin Shift	Rankin Shift
Imaging Modality	NCCT, CTA, CTP or MRI/MRA/PWI	NCCT, CTA , CTP Mismatch	CTA or MRA, ASPECTS	NCCT, CTA, Collateral assessment on multiplhase CTA ASPECTS	ASPECTS
Median NIHSS	17/17	13/17	17/17	17/16	18/17
Primary Device Studied	Solitaire™ Device	Solitaire™ Device	Solitaire™ Device	Solitaire™ Device	Stent retrievers
Statistically Significant Benefit	✓	✓	✓	✓	✓

DEFUSE-3 Trial





G. Zaharchuk, S. Kim, J. Carrozzella, Y.Y. Palesch, A.M. Demchuk, R. Bammer, P.W. Lavori, J.P. Broderick, and M.G. Lansberg, for the DEFUSE 3 Investigators*



Inclusion criteria

Eligible 6-16h after last seen well

Occlusion of extracranial or intracranial ICA or proximal MCA

Infarct volume <70 ml+Ratio of volume of ischemic tissue to initial infarct volume of ≥1.8

CT or MRI based imaging

RAPID software for image analysis

All FDA-approved devices for recanalization allowed

Sponsor: NIH

Αποτελεσματική η θρομβεκτομή εντός 6-16 ωρών με ΑΕΕ από απόφραξη έσω καρωτίδας/ μέσης εγκεφαλικής αρτηρίας σε επιλεγμένους ασθενείς με βάση συγκεκριμένα απεικονιστικά χαρακτηριστικά

DAWN trial

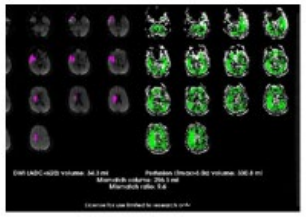
The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JANUARY 4, 2018 VOL. 378 NO. 1

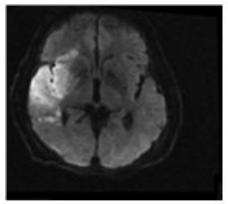
Thrombectomy 6 to 24 Hours after Stroke with a Mismatch between Deficit and Infarct

R.G. Nogueira, A.P. Jadhav, D.C. Haussen, A. Bonafe, R.F. Budzik, P. Bhuva, D.R. Yavagal, M. Ribo, C. Cognard, R.A. Hanel, C.A. Sila, A.E. Hassan, M. Millan, E.I. Levy, P. Mitchell, M. Chen, J.D. English, Q.A. Shah, F.L. Silver, V.M. Pereira, B.P. Mehta, B.W. Baxter, M.G. Abraham, P. Cardona, E. Veznedaroglu, F.R. Hellinger, L. Feng, J.F. Kirmani, D.K. Lopes, B.T. Jankowitz, M.R. Frankel, V. Costalat, N.A. Vora, A.J. Yoo, A.M. Malik, A.J. Furlan, M. Rubiera, A. Aghaebrahim, J.-M. Olivot, W.G. Tekle, R. Shields, T. Graves, R.J. Lewis, W.S. Smith, D.S. Liebeskind, J.L. Saver, and T.G. Jovin, for the DAWN Trial Investigators*

Mismatch: Stroke severity/Imaging

- Clinical Severity
  - NIHSS (0-42)
    - 0: No stroke symptoms
    - 1-4: Minor stroke
    - 5-15: Moderate stroke
    - 16-20: Moderate to severe stroke
    - 21-42: Severe stroke
- Infarct Volume





Inclusion criteria

Eligible 6-24h after last seen well
Occlusion of intracranial ICA or proximal MCA
Group A: >80y, NIHSS≥10, infarct volume <21 ml
Group B: <80y, NIHSS≥10, infarct volume <31 ml
Group C: <80y, NIHSS ≥20, infarct volume 31-50 ml
CT or MRI based imaging
RAPID software for image analysis
Only TREVO device allowed for recanalization

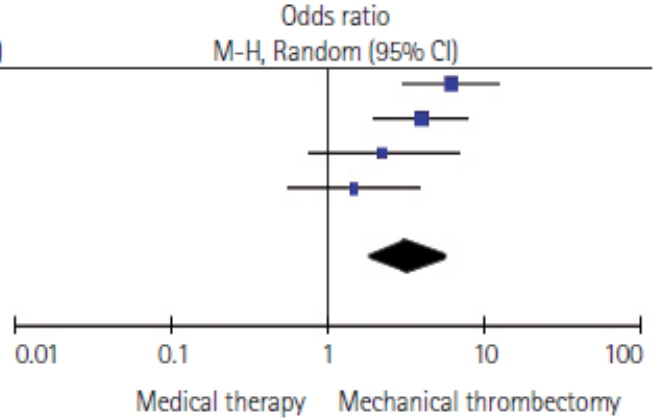
- For every 100 patients treated with endovascular therapy, 49 will have a less disabled outcome as a results of treatment, including 36 who were functionally independent
- The treatment effect size in DAWN is the highest out of any stroke trials to date and suggests that the presence of Clinical-Core Mismatch is a critical predictor of treatment effect independent of time

Thrombectomy beyond 6 hours

Study or subgroup	Mechanical thrombectomy Events	Total	Medical therapy Events	Total	Weight (%)	Odds ratio M-H, Random (95% CI)
DAWN 2018	52	107	13	99	29.7	6.25 (3.12–12.54)
DEFUSE 3 2018	41	92	15	90	29.9	4.02 (2.02–8.02)
ESCAPE 2018	16	33	7	24	18.5	2.29 (0.75–6.96)
REVASCAT 2015	15	35	12	36	21.9	1.50 (0.57–3.93)
Total (95% CI)		267		249	100.0	3.33 (1.81–6.12)
Total events	124		47			

Heterogeneity: $Tau^2=0.20$, $Chi^2=6.33$, df=3 ($p=0.10$), $I^2=53\%$

Test for overall effect: $Z=3.86$ ($p=0.0001$)



Vidale et al. J Clin Neurology 2018

AHA/ASA Guideline

2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

3.7. Mechanical Thrombectomy (Continued)	COR	LOE	New, Revised, or Unchanged
7. In selected patients with AIS within 6 to 16 hours of last known normal who have LVO in the anterior circulation and meet other DAWN or DEFUSE 3 eligibility criteria, mechanical thrombectomy is recommended.	I	A	New recommendation.
8. In selected patients with AIS within 6 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.	IIa	B-R	New recommendation.

AHA/ASA guidelines 2018

AHA/ASA Guideline

2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

3.7. Mechanical Thrombectomy (Continued)	COR	LOE	New, Revised, or Unchanged
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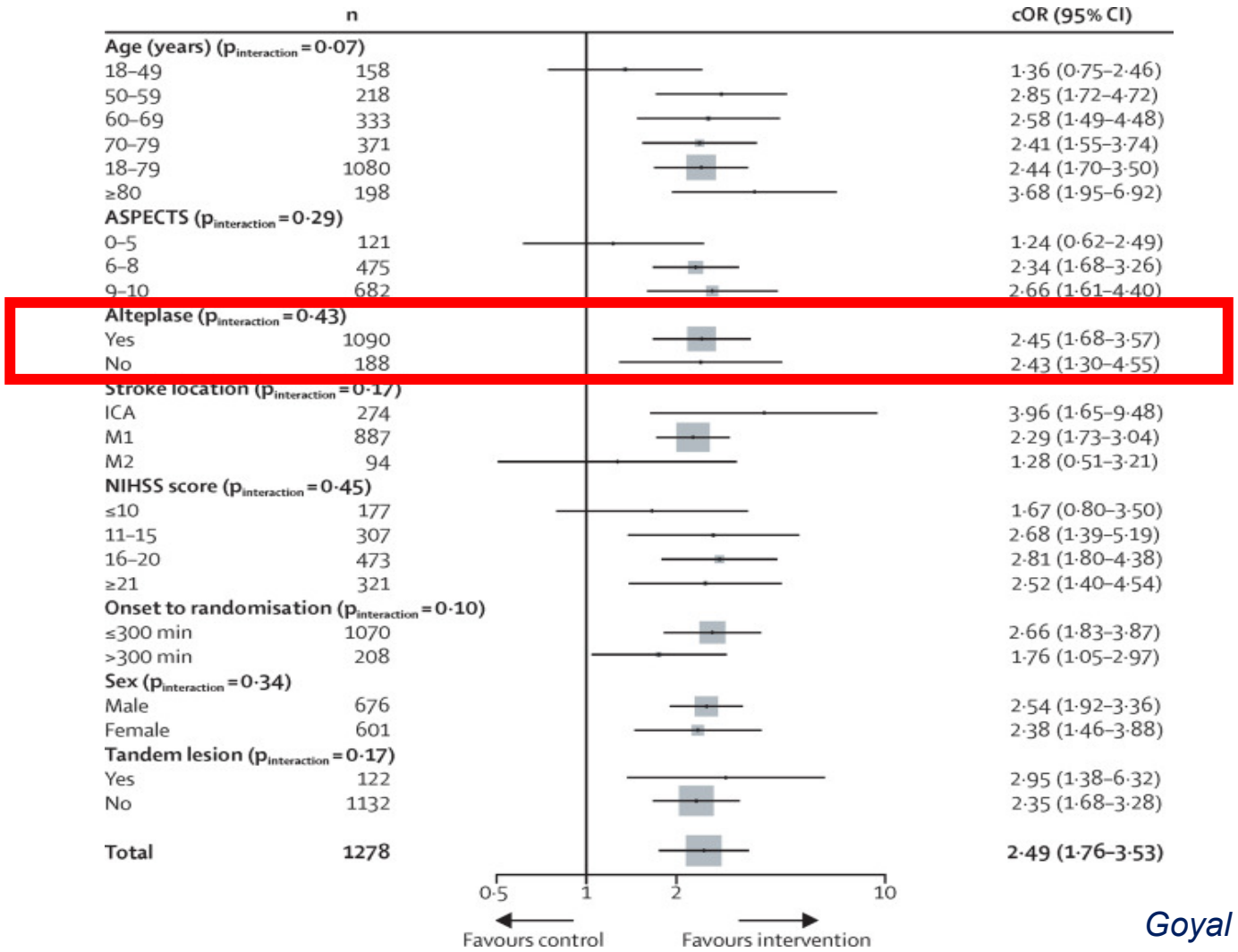
8. In selected patients with AIS within 6 to 24 hours of last known normal who have LVO in the anterior circulation and meet other DAWN eligibility criteria, mechanical thrombectomy is reasonable.	IIa	B-R	New recommendation.

AHA/ASA guidelines 2019

Subgroup analysis *(HERMES)*



Goyal M, et al. Lancet. 2016;387:1723-31

IVT before EVT: limitations

- IVT might delay the start of EVT
- IVT may cause partial lysis and migration of thrombus to a more distal arterial segment (beyond the reach of EVT)
- IVT may increase the frequency of hemorrhagic transformation
- Angioplasty and stenting during EVT requires DAPT for stent protection during the first 24h

Myocardial Infarction: PCI vs Facilitated PCI

Primary versus tenecteplase-facilitated percutaneous coronary intervention in patients with ST-segment elevation acute myocardial infarction (ASSENT-4 PCI): randomised trial

*Assessment of the Safety and Efficacy of a New Treatment Strategy with Percutaneous Coronary Intervention (ASSENT-4 PCI) investigators**

Summary

Background Primary percutaneous coronary intervention (PCI) is more effective than fibrinolytic therapy for ST-segment elevation acute myocardial infarction (STEMI), but time to intervention can be considerable. Our aim was to investigate whether the administration of full-dose tenecteplase before a delayed PCI could mitigate the

Lancet 2006; 367: 569–78
Published **Online**
February 14, 2006

Comparison of primary and facilitated percutaneous coronary interventions for ST-elevation myocardial infarction: quantitative review of randomised trials

Ellen C Keeley, Judith A Boura, Cindy L Grines

Summary

Background Facilitated percutaneous coronary intervention for ST-segment-elevation myocardial infarction (STEMI) is defined as the use of pharmacological substances before a planned immediate intervention, to improve coronary patency. We undertook a meta-analysis of randomised controlled trials (published and unpublished) to compare facilitated and primary percutaneous coronary intervention.

Methods We identified 17 trials of patients with STEMI assigned to facilitated (n=2237) or primary (n=2267) percutaneous coronary intervention. We identified short-term outcomes (up to 42 days) of death, stroke, non-fatal reinfarction, urgent target vessel revascularisation, and major bleeding. Grade 3 flow rates for prethrombolysis and post-thrombolysis in myocardial infarction (TIMI) were also analysed.

Findings The facilitated approach resulted in a greater than two-fold increase in the number of patients with initial TIMI grade 3 flow, compared with the primary approach (832 patients [37%] *vs* 342 [15%], odds ratio 3·18, 95% CI 2·22–4·55); however, final rates did not differ (1706 [89%] *vs* 1803 [88%]; 1·19, 0·86–1·64). Significantly more patients assigned to the facilitated approach than those assigned to the primary approach died (106 [5%] *vs* 78 [3%]; 1·38, 1·01–1·87), had higher non-fatal reinfarction rates (74 [3%] *vs* 41 [2%]; 1·71, 1·16–2·51), and had higher urgent target vessel revascularisation rates (66 [4%] *vs* 21 [1%]; 2·39, 1·23–4·66); the increased rates of adverse events seen with the facilitated approach were mainly seen in thrombolytic-therapy-based regimens. Facilitated intervention was associated with higher rates of major bleeding than primary intervention (159 [7%] *vs* 108 [5%]; 1·51, 1·10–2·08). Haemorrhagic stroke and total stroke rates were higher in thrombolytic-therapy-containing facilitated regimens than in primary intervention (haemorrhagic stroke 15 [0·7%] *vs* two [0·1%], p=0·0014; total stroke 24 [1·1%] *vs* six [0·3%], p=0·0008).

Interpretation Facilitated percutaneous coronary intervention offers no benefit over primary percutaneous coronary intervention in STEMI treatment and should not be used outside the context of randomised controlled trials. Furthermore, facilitated interventions with thrombolytic-based regimens should be avoided.

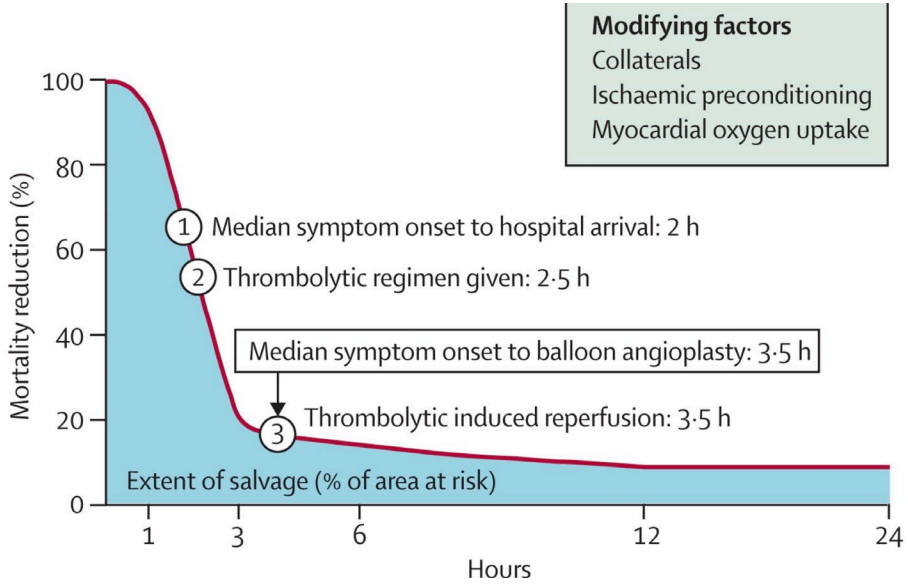
Lancet 2006; 367: 579–88
Published **Online**
February 14, 2006
DOI:10.1016/S0140-6736(06)68148-8
See **Comment** page 543

Department of Internal Medicine, Division of Cardiology, University of Texas Southwestern Medical Center, Dallas, TX 75390-9047, USA (E C Keeley MD); **and William Beaumont Hospital, Royal Oak, MI, USA** (J A Boura MS, C L Grines MD)
Correspondence to:
Dr Ellen C Keeley
Ellen.Keeley@UTSouthwestern.edu

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 MAY 22, 2008 VOL. 358 NO. 21

Facilitated PCI in Patients with ST-Elevation Myocardial Infarction

Stephen G. Ellis, M.D., Michal Tendera, M.D., Mark A. de Belder, M.D., Ad J. van Boven, M.D., Petr Widimsky, M.D., Luc Janssens, M.D., H.R. Andersen, M.D., Amadeo Betriu, M.D., Stefano Savonitto, M.D., Jerzy Adamus, M.D., Jan Z. Peruga, M.D., Maciej Kosmider, M.D., Olivier Katz, M.D., Thomas Neunteufl, M.D., Julia Jorgova, M.D., Maria Dorobantu, M.D., Liliana Grinfeld, M.D., Paul Armstrong, M.D., Bruce R. Brodie, M.D., Howard C. Herrmann, M.D., Gilles Montalescot, M.D., Franz-Josef Neumann, M.D., Mark B. Effron, M.D., Elliot S. Barnathan, M.D., and Eric J. Topol, M.D., for the FINESSE Investigators*



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 NOVEMBER 11, 2021 VOL. 385 NO. 20

A Randomized Trial of Intravenous Alteplase before Endovascular Treatment for Stroke

N.E. LeCouffe, M. Kappelhof, K.M. Treurniet, L.A. Rinkel, A.E. Bruggeman, O.A. Berkhemer, L. Wolff, H. van Voorst, M.L. Tolhuisen, D.W.J. Dippel, A. van der Lugt, A.C.G.M. van Es, J. Boiten, G.J. Lycklama à Nijeholt, K. Keizer, R.A.R. Gons, L.S.F. Yo, R.J. van Oostenbrugge, W.H. van Zwam, B. Roozenbeek, H.B. van der Worp, R.T.H. Lo, I.R. van den Wijngaard, I.R. de Ridder, V. Costalat, C. Arquizan, R. Lemmens, J. Demeestere, J. Hofmeijer, J.M. Martens, W.J. Schonewille, J.-A. Vos, M. Uyttenboogaart, R.P.H. Bokkers, J.H. van Tuijl, H. Kortman, F.H.B.M. Schreuder, H.D. Boogaarts, K.F. de Laat, L.C. van Dijk, H.M. den Hertog, B.A.A.M. van Hasselt, P.J.A.M. Brouwers, T. Bulut, M.J.M. Remmers, A. van Norden, F. Imani, A.D. Rozeman, O.E.H. Elgersma, P. Desfontaines, D. Brisbois, Y. Samson, F. Clarençon, G.M. Krietemeijer, A.A. Postma, P.-J. van Doormaal, R. van den Berg, A. van der Hoorn, L.F.M. Beenen, D. Nieboer, H.F. Lingsma, B.J. Emmer, J.M. Coutinho, C.B.L.M. Majoie, and Y.B.W.E.M. Roos, for the MR CLEAN–NO IV Investigators*

Research

JAMA | Original Investigation

Effect of Endovascular Treatment Alone vs Intravenous Alteplase Plus Endovascular Treatment on Functional Independence in Patients With Acute Ischemic Stroke The DEVT Randomized Clinical Trial

Wenjie Zi, MD; Zhongming Qiu, MD; Fengli Li, MD; Hongfei Sang, MD; Deping Wu, MD; Weidong Luo, MD; Shuai Liu, MD; Junjie Yuan, MD; Jiaxing Song, MD; Zhonghua Shi, MD; Wenguo Huang, MD; Min Zhang, MS; Wenhua Liu, MD; Zhangbao Guo, MS; Tao Qiu, MD; Qiang Shi, MS; Peiyang Zhou, MD; Li Wang, MD; Xinmin Fu, MD; Shudong Liu, MD; Shiquan Yang, MD; Shuai Zhang, MD; Zhiming Zhou, MD; Xianjun Huang, MD; Yan Wang, MD; Jun Luo, MS; Yongjie Bai, MD; Min Zhang, MS; Youlin Wu, MS; Guoyong Zeng, MD; Yue Wan, MD; Changming Wen, MD; Hongbin Wen, MD; Wentong Ling, MS; Zhuo Chen, MS; Miao Peng, MS; Zhibing Ai, MD; Fuqiang Guo, MD; Huagang Li, MD; Jing Guo, MS; Haitao Guan, MD; Zhiyi Wang, MS; Yong Liu, MS; Jie Pu, MD; Zhen Wang, MD; Hansheng Liu, MD; Luming Chen, MD; Jiacheng Huang, MD; Guoqiang Yang, MD; Zili Gong, MD; Jie Shuai, MD; Raul G. Nogueira, MD; Qingwu Yang, MD, PhD; for the DEVT Trial Investigators

IMPORTANCE For patients with large vessel occlusion strokes, it is unknown whether endovascular treatment alone compared with intravenous thrombolysis plus endovascular treatment (standard treatment) can achieve similar functional outcomes.

OBJECTIVE To investigate whether endovascular thrombectomy alone is noninferior to intravenous alteplase followed by endovascular thrombectomy for achieving functional independence at 90 days among patients with large vessel occlusion stroke.

DESIGN, SETTING, AND PARTICIPANTS Multicenter, randomized, noninferiority trial conducted at 33 stroke centers in China. Patients (n = 234) were 18 years or older with proximal anterior circulation intracranial occlusion strokes within 4.5 hours from symptoms onset and eligible for intravenous thrombolysis. Enrollment took place from May 20, 2018, to May 2, 2020. Patients were enrolled and followed up for 90 days (final follow-up was July 22, 2020).

INTERVENTIONS A total of 116 patients were randomized to the endovascular thrombectomy alone group and 118 patients to combined intravenous thrombolysis and endovascular thrombectomy group.

MAIN OUTCOMES AND MEASURES The primary end point was the proportion of patients achieving functional independence at 90 days (defined as score 0-2 on the modified Rankin Scale; range, 0 [no symptoms] to 6 [death]). The noninferiority margin was −10%. Safety outcom and 90-

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Multimedia
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Supplemental content
CME Quiz at jamacmelookup.com

JAMA | Original Investigation

Effect of Mechanical Thrombectomy Without vs With Intravenous Thrombolysis on Functional Outcome Among Patients With Acute Ischemic Stroke The SKIP Randomized Clinical Trial

Kentaro Suzuki, MD, PhD; Yuji Matsumaru, MD, PhD; Masataka Takeuchi, MD; Masafumi Morimoto, MD, PhD; Ryuzaburo Kanazawa, MD, PhD; Yohei Takayama, MD; Yuki Kamiya, MD, PhD; Keigo Shigeta, MD, PhD; Seiji Okubo, MD, PhD; Mikito Hayakawa, MD; Norihiro Ishii, MD, PhD; Yorio Koguchi, MD, PhD; Tomoji Takigawa, MD, PhD; Masato Inoue, MD, PhD; Hiromichi Naito, MD; Takahiro Ota, MD, PhD; Teruyuki Hirano, MD, PhD; Noriyuki Kato, MD, PhD; Toshihiro Ueda, MD, PhD; Yasuyuki Iguchi, MD, PhD; Kazunori Akaji, MD, PhD; Wataro Tsuruta, MD, PhD; Kazunori Miki, MD, PhD; Shigeru Fujimoto, MD, PhD; Tetsuhiro Higashida, MD, PhD; Mitsuhiro Iwasaki, MD; Junya Aoki, MD, PhD; Yasuhiro Nishiyama, MD, PhD; Toshiaki Otsuka, MD, PhD; Kazumi Kimura, MD, PhD; for the SKIP Study Investigators

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 21, 2020 VOL. 382 NO. 21

Endovascular Thrombectomy with or without Intravenous Alteplase in Acute Stroke

P. Yang, Yongwei Zhang, L. Zhang, Yongxin Zhang, K.M. Treurniet, W. Chen, Y. Peng, H. Han, J. Wang, S. Wan C. Yin, S. Liu, P. Wang, Q. Fang, Hongchao Shi, J. Yang, C. Wen, C. Li, C. Jiang, J. Sun, X. Yue, M. Lou, M. Zhan H. Shu, D. Sun, H. Liang, Tong Li, F. Guo, K. Ke, H. Yuan, G. Wang, W. Yang, Huaizhang Shi, Tianxiao Li, Z. L P. Xing, P. Zhang, Y. Zhou, H. Wang, Y. Xu, Q. Huang, T. Wu, R. Zhao, Q. Li, Y. Fang, Laixing Wang, J. Lu, Y. L J. Fu, X. Zhong, Y. Wang, Longde Wang, M. Goyal, D.W.J. Dippel, B. Hong, B. Deng, Y.B.W.E.M. Roos, C.B.L.M. Majoie, and J. Liu, for the DIRECT-MT Investigators*

ABSTRACT

BACKGROUND
In acute ischemic stroke, there is uncertainty regarding the benefit and risk of administering intravenous alteplase before endovascular thrombectomy.

METHODS
We conducted a trial at 41 academic tertiary care centers in China to evaluate endovascular thrombectomy with or without intravenous alteplase in patients with acute ischemic stroke. Patients with acute ischemic stroke from large-vessel occlusion in the anterior circulation were randomly assigned in a 1:1 ratio to undergo endovascular thrombectomy alone (thrombectomy-alone group) or endovascular thrombectomy preceded by intravenous alteplase, at a dose of 0.9 mg per kilogram of body weight, administered within 4.5 hours after symptom onset (combination-therapy group). The primary analysis for ence in the distribution of the mo to 6 [death]) at 90 days on the l interval of the adjusted common various secondary outcomes, incl

RESULTS
Of 1586 patients screened, 656 thrombectomy-alone group and Endovascular thrombectomy alo teplase and endovascular thror (adjusted common odds ratio, 1. for noninferiority) but was assoc cessful reperfusion before thror reperfusion (79.4% vs. 84.5%). N my-alone group and 18.8% in th

CONCLUSIONS
In Chinese patients with acute is vascular thrombectomy alone wa within a 20% margin of confide intravenous alteplase administer by the Stroke Prevention Project Republic of China and the Wu J Trials.gov number, NCT03469206

The authors' full names, academi groups, and affiliations are listed i Appendix. Address reprint reques Dr. J. Liu at the Department of Neur gery, Changhai Hospital, 168 Changhu Shanghai 200433, China, or at direct_ 163.com.

*A complete list of the DIRECT-MT I tigators and collaborators is provid the Supplementary Appendix, avai at NEJM.org.

Drs. P. Yang and Yongwei Zhang and

Articles

Endovascular thrombectomy versus standard bridging thrombolytic with endovascular thrombectomy within 4·5 h of stroke onset: an open-label, blinded-endpoint, randomised non-inferiority trial

Peter J Mitchell*, Bernard Yan*, Leonid Churilov, Richard J Dowling, Steven J Bush, Andrew Bivard, Xiao Chuan Huo, Guoqing Wang, Shi Yong Zhang, Mai Duy Ton, Dennis J Cordato, Timothy J Kleinig, Henry Ma, Ronil V Chandra, Helen Brown, Bruce C V Campbell, Andrew K Cheung, Brendan Steinfort, Rebecca Scroop, Kendal Redmond, Ferdinand Miteff, Yan Liu, Dang Phuc Duc, Hal Rice, Mark W Parsons, Teddy Y Wu, Huy-Thang Nguyen, Geoffrey A Donnan†, Zhong Rong Miao†, Stephen M Davis†, on behalf of the DIRECT-SAFE Investigators‡

Lancet 2022; 400: 116–25
See Comment page 76

*Joint principal investigators
†Joint senior authors
‡Investigators listed at the end of the report
Department of Radiology (Prof P J Mitchell MMed, R J Dowling MBBS, S J Bush MBBS), Department of Medicine and Neurology, Melbourne Brain Centre (Prof B Yan DMedSci, A Bivard PhD, Prof B C V Campbell PhD,

Summary

Background The benefit of combined treatment with intravenous thrombolysis before endovascular thrombectomy in patients with acute ischaemic stroke caused by large vessel occlusion remains unclear. We hypothesised that the clinical outcomes of patients with stroke with large vessel occlusion treated with direct endovascular thrombectomy within 4·5 h would be non-inferior compared with the outcomes of those treated with standard bridging therapy (intravenous thrombolysis before endovascular thrombectomy).

Methods DIRECT-SAFE was an international, multicentre, prospective, randomised, open-label, blinded-endpoint trial. Adult patients with stroke and large vessel occlusion in the intracranial internal carotid artery, middle cerebral artery (M1 or M2), or basilar artery, confirmed by non-contrast CT and vascular imaging, and who presented within 4·5 h of stroke onset were recruited from 25 acute-care hospitals in Australia, New Zealand, China, and Vietnam. Eligible patients were randomly assigned (1:1) via a web-based, computer-generated randomisation procedure stratified by site of baseline arterial occlusion and by geographic region to direct endovascular thrombectomy or bridging therapy. Patients assigned to bridging therapy received intravenous thrombolytic (alteplase or tenecteplase) as per standard care at each site; endovascular thrombectomy was also per standard of care, using the Trevo device (Stryker Neurovascular, A) as first-line intervention. Personnel assessing outcomes were masked to group allocation; patients icians were not. The primary efficacy endpoint was functional independence defined as modified e 0–2 or return to baseline at 90 days, with a non-inferiority margin of −0·1, analysed by intention to l randomly assigned and consenting patients) and per protocol. The intention-to-treat population was afety analyses. The trial is registered with ClinicalTrials.gov, NCT03494920, and is closed to new

June 2, 2018, and July 8, 2021, 295 patients were randomly assigned to direct endovascular =148) or bridging therapy (n=147). Functional independence occurred in 80 (55%) of 146 patients in ectomy group and 89 (61%) of 147 patients in the bridging therapy group (intention-to-treat risk l, two-sided 95% CI −0·160 to 0·059; per-protocol risk difference −0·062, two-sided 95% CI Safety outcomes were similar between groups, with symptomatic intracerebral haemorrhage occurring 6 patients in the direct group and one (1%) of 147 patients in the bridging group (adjusted odds l 0·22–13·04) and death in 22 (15%) of 146 patients in the direct group and 24 (16%) of 147 patients in p (adjusted odds ratio 0·92, 95% CI 0·46–1·84).

did not show non-inferiority of direct endovascular thrombectomy compared with bridging therapy. formation from our study should inform guidelines to recommend bridging therapy as standard

n National Health and Medical Research Council and Stryker USA.

five randomised controlled studies avenous thrombolysis alone with g intravenous thrombolysis followed by mbectomy showed a clear superiority of combined bridging therapy.[3-5] A subsequent pooled analysis (HERMES)[6] confirmed the beneficial effects of endovascular thrombectomy that extended across a spectrum of subgroups, with over 80% of these patients having bridging therapy with alteplase.[6] The use of

Protocol

SWIFT DIRECT: Solitaire™ With the Intention For Thrombectomy Plus Intravenous t-PA Versus DIRECT Solitaire™ Stent-retriever Thrombectomy in Acute Anterior Circulation Stroke: Methodology of a randomized, controlled, multicentre study

Urs Fischer[1], Johannes Kaesmacher[2], Patricia S Plattner[2], Lukas Bütikofer[3], Pasquale Mordasini[2], Sandro Deppeler[2], Christoph Cognard[4], Vitor M Pereira[5], Adnan H Siddiqui[6], Michael T Froehler[7], Anthony J Furlan[8], René Chapot[9], Daniel Strbian[10], Martin Wiesmann[11], Jenny Bressan[1], Stefanie Lerch[1], David S Liebeskind[13], Jeffery L Saver[12] and Jan Gralla[2]; on behalf of the SWIFT DIRECT study investigators

International Journal of Stroke
2022, Vol. 17(6) 698–705

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atment with intravenous alteplase prior to mechanical thrombectomy (MT) in acute ischemic

SWIFT DIRECT

ESOC Official Welcome & Large Clinical Trials

terventional Neuroradiology, University , Bern, Switzerland
Bern, Switzerland
Therapeutic Neuroradiology, University France
Division of Neurosurgery, Departments , Toronto Western Hospital, University Toronto, Toronto, Canada
nd Toshiba Stroke and Vascular Research York at Buffalo, Buffalo, USA
rogram, Vanderbilt University Medical Krankenhaus Essen, Essen, Germany
[10]Department of Neurology, Helsinki University Hospital and University of Helsinki, Helsinki, Finland
[11]Department of Neuroradiology, University Hospital RWTH Aachen, Aachen, Germany
[12]Department of Neurology and Comprehensive Stroke Center, David Geffen School of Medicine, University of California, Los Angeles, USA
[13]Department of Neurology and UCLA Stroke Center, Los Angeles, California, USA
Corresponding author:
Urs Fischer, Department of Neurology, Inselspital, Freiburgstrasse 8, CH-3010 Bern, Switzerland.
Email: urs.fischer@insel.ch

DIRECT SAFE

GUIDELINES

2022 Brief Practice Update on Intravenous Thrombolysis Before Thrombectomy in Patients With Large Vessel Occlusion Acute Ischemic Stroke: A Statement from Society of Vascular and Interventional Neurology Guidelines and Practice Standards (GAPS) Committee

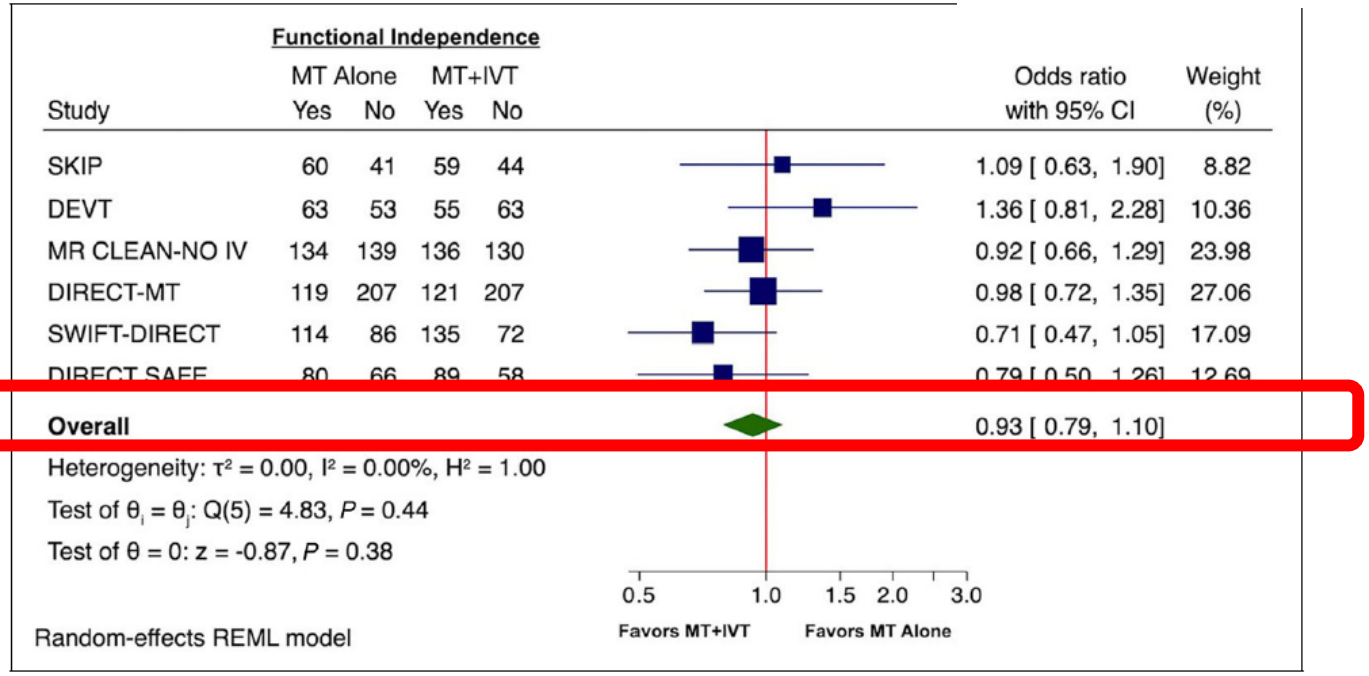
Recommendations

- In patients with large vessel occlusion-related ischemic stroke eligible for both treatments, we recommend intravenous thrombolysis plus mechanical thrombectomy over mechanical thrombectomy alone. Both treatments should be performed as early as possible after hospital arrival. Mechanical thrombectomy should not prevent the initiation of intravenous thrombolysis, and intravenous thrombolysis should not delay mechanical thrombectomy.

Quality of evidence: **Very low** ⨁; strength of recommendation: **Strong** ↑↑

- In patients with large vessel occlusion-related ischemic stroke not eligible for intravenous thrombolysis, we recommend mechanical thrombectomy as stand-alone treatment.

Quality of evidence: **Low** ⨁⨁; strength of recommendation: **Strong** ↑↑



RESEARCH SUMMARY

Endovascular Therapy for Stroke Due to Basilar-Artery Occlusion

Langezaal LCM et al. DOI: 10.1056/NEJMoa2030297

CLINICAL PROBLEM

Basilar-artery occlusion, which accounts for approximately 10% of all ischemic strokes caused by intracranial proximal large-vessel occlusion, is associated with high morbidity and mortality. The effectiveness of endovascular therapy in patients with stroke caused by basilar-artery occlusion has not been well studied.

CLINICAL TRIAL

Design: A multicenter, open-label, international, randomized, controlled trial with blinded outcome assessment.

Intervention: 300 patients were assigned within 6 hours after the estimated time of onset of a stroke due to basilar-artery occlusion, in a 1:1 ratio, to receive endovascular therapy or standard medical care. The primary outcome was a favorable functional outcome (a score of 0 to 3 on the modified Rankin scale; range, 0 to 6, with 0 indicating no disability, 3 indicating moderate disability, and 6 indicating death) at 90 days.

RESULTS

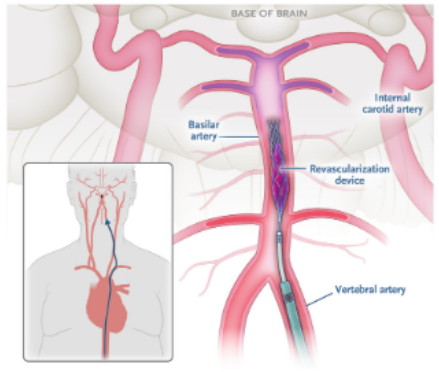
Efficacy: Approximately 80% of patients in each group received intravenous thrombolysis. The results did not show a significant difference in favorable functional outcome between the two groups, but the width of the confidence interval may not exclude a benefit of endovascular therapy.

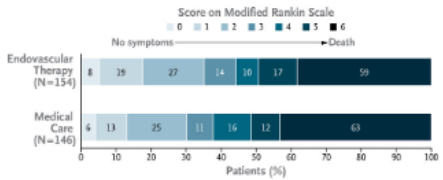
Safety: Symptomatic intracranial hemorrhage occurred in 4.5% of the patients after endovascular therapy and in 0.7% of those after medical therapy (risk ratio, 6.9; 95% CI, 0.9 to 53.0). There was no significant difference in mortality at 90 days.

LIMITATIONS AND REMAINING QUESTIONS

- Larger trials are needed to determine the efficacy and safety of endovascular therapy for basilar-artery occlusion.
- Recruitment of patients for trials of treatment for basilar-artery occlusion is difficult.
- Recruitment was lower than anticipated, so the trial was underpowered for some analyses, including subgroup analyses.

Links: Full article | NEJM Quick Take | Editorial





Outcomes

	Endovascular Therapy (N=154)	Medical Care (N=146)	Risk Ratio, Common Odds Ratio, or Mean Difference (95% CI)
Primary outcome at day 90 Modified Rankin scale score ≤3	44.2%	37.7%	1.18 (0.92 to 1.50)
Serious adverse events			
Symptomatic intracranial hemorrhage ≤3 days after initiation of treatment	4.5%	0.7%	
Malignant brain edema	11.0%	4.8%	
Subarachnoid or intraventricular hemorrhage on CT at 24 hr	4/129	1/115	

CONCLUSIONS

In patients with basilar-artery occlusion, endovascular therapy and medical therapy were not significantly different with respect to a favorable functional outcome.

European Stroke Organisation (ESO) - European Society for Minimally Invasive Neurological Therapy (ESMINT) Guidelines on Mechanical Thrombectomy in Acute Ischemic Stroke

Guillaume Turc,[1,2,3,4] Pervinder Bhogal,[5] Urs Fischer,[6] Pooja Khatri,[7] Kyriakos Lobotesis,[8] Mikaël Mazighi,[3,9,10,11] Peter D. Schellinger,[12] Danilo Toni,[13] Joost de Vries,[14] Philip White,[15] Jens Fiehler[16]

Expert opinion on mechanical thrombectomy for basilar artery occlusion

There is a consensus among the panel (11/11 votes) that in analogy to anterior circulation large vessel occlusion and with regard to the grim natural course of basilar artery occlusions, the therapeutic approach with intravenous thrombolysis plus mechanical thrombectomy should strongly be considered.

Θρομβεκτομή στη βασική αρτηρία

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ORIGINAL ARTICLE

Trial of Endovascular Treatment of Acute Basilar-Artery Occlusion

C. Tao, R.G. Nogueira, Y. Zhu, J. Sun, H. Han, G. Yuan, C. Wen, P. Zhou, W. Chen, G. Zeng, Y. Li, Z. Ma, C. Yu, J. Su, Z. Zhou, Z. Chen, G. Liao, Y. Sun, Y. Ren, H. Zhang, J. Chen, X. Yue, G. Xiao, Li Wang, R. Liu, W. Liu, Y. Liu, Li Wang, C. Zhang, T. Liu, J. Song, R. Li, P. Xu, Y. Yin, G. Wang, B. Baxter, A.I. Qureshi, X. Liu, and W. Hu, for the ATTENTION Investigators*

ABSTRACT

BACKGROUND

Data from trials investigating the effects and risks of endovascular thrombectomy for the treatment of stroke due to basilar-artery occlusion are limited.

METHODS

We conducted a multicenter, prospective, randomized, controlled trial of endovascular thrombectomy for basilar-artery occlusion at 36 centers in China. Patients were assigned, in a 2:1 ratio, within 12 hours after the estimated time of basilar-artery occlusion to receive endovascular thrombectomy or best medical care (control). The primary outcome was good functional status, defined as a score of 0 to 3 on the modified Rankin scale (range, 0 [no symptoms] to 6 [death]), at 90 days. Secondary outcomes included a modified Rankin scale score of 0 to 2, distribution across the modified Rankin scale score categories, and quality of life. Safety outcomes included symptomatic intracranial hemorrhage at 24 to 72 hours, 90-day mortality, and procedural complications.

RESULTS

Of the 507 patients who underwent screening, 340 were in the intention-to-treat population, with 226 assigned to the thrombectomy group and 114 to the control group. Intravenous thrombolysis was used in 31% of the patients in the thrombectomy group and in 34% of those in the control group. Good functional status at 90 days occurred in 104 patients (46%) in the thrombectomy group and in 26 (23%) in the control group (adjusted rate ratio, 2.06; 95% confidence interval [CI], 1.46 to 2.91, P<0.001). Symptomatic intracranial hemorrhage occurred in 12 patients (5%) in the thrombectomy group and in none in the control group. Results for the secondary clinical and imaging outcomes were generally in the same direction as those for the primary outcome. Mortality at 90 days was 37% in the thrombectomy group and 55% in the control group (adjusted risk ratio, 0.66; 95% CI, 0.52 to 0.82). Procedural complications occurred in 14% of the patients in the thrombectomy group, including one death due to arterial perforation.

CONCLUSIONS

In a trial involving Chinese patients with basilar-artery occlusion, approximately one third of whom received intravenous thrombolysis, endovascular thrombectomy within 12 hours after stroke onset led to better functional outcomes at 90 days than best medical care but was associated with procedural complications and intracerebral hemorrhage. (Funded by the Program for Innovative Research Team of the First Affiliated Hospital of USTC and others; ATTENTION ClinicalTrials.gov number, NCT04751708.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Hu can be contacted at andinghu@126.com or at the Stroke Center and Department of Neurology, First Affiliated Hospital of USTC, 17 Lujiang Rd., Hefei 230001, China.

*A list of the investigators in the ATTENTION trial is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Tao, Nogueira, Zhu, and Han, and Drs. X. Liu and Hu, contributed equally to this article.

ORCID information for Dr. Li Wang of Zigong Third People's Hospital, Zigong, and for Dr. Li Wang of the First Affiliated Hospital of USTC, Hefei, is available at https://orcid.org/0000-0002-6484-9323 and https://orcid.org/0000-0002-0527-7835, respectively.

N Engl J Med 2022;387:1361-72.
DOI: 10.1056/NEJMoa2206317

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Trial of Thrombectomy 6 to 24 Hours after Stroke Due to Basilar-Artery Occlusion

T.G. Jovin, C. Li, L. Wu, C. Wu, Jian Chen, C. Jiang, Z. Shi, Z. Gao, C. Song, W. Chen, Y. Peng, C. Yao, M. Wei, T. Li, L. Wei, G. Xiao, H. Yang, M. Ren, J. Duan, X. Liu, Qingwu Yang, Y. Liu, Qingfeng Zhu, W. Shi, Qiyi Zhu, X. Li, Z. Guo, Qi Yang, C. Hou, W. Zhao, Q. Ma, Y. Zhang, L. Jiao, H. Zhang, D.S. Liebeskind, H. Liang, A.P. Jadhav, C. Wen, S. Brown, L. Zhu, H. Ye, M. Ribo, M. Chang, H. Song, Jun Chen, and X. Ji, for the BAOCHE Investigators*

ABSTRACT

BACKGROUND

The effects and risks of endovascular thrombectomy 6 to 24 hours after stroke onset due to basilar-artery occlusion have not been extensively studied.

METHODS

In a trial conducted over a 5-year period in China, we randomly assigned, in a 1:1 ratio, patients with basilar-artery stroke who presented between 6 to 24 hours after symptom onset to receive either medical therapy plus thrombectomy or medical therapy only (control). The original primary outcome, a score of 0 to 4 on the modified Rankin scale (range, 0 to 6, with a score of 0 indicating no disability, 4 moderately severe disability, and 6 death) at 90 days, was changed to a good functional status (a modified Rankin scale score of 0 to 3, with a score of 3 indicating moderate disability). Primary safety outcomes were symptomatic intracranial hemorrhage at 24 hours and 90-day mortality.

RESULTS

A total of 217 patients (110 in the thrombectomy group and 107 in the control group) were included in the analysis; randomization occurred at a median of 663 minutes after symptom onset. Enrollment was halted at a prespecified interim analysis because of the superiority of thrombectomy. Thrombolysis was used in 14% of the patients in the thrombectomy group and in 21% of those in the control group. A modified Rankin scale score of 0 to 3 (primary outcome) occurred in 51 patients (46%) in the thrombectomy group and in 26 (24%) in the control group (adjusted rate ratio, 1.81; 95% confidence interval [CI], 1.26 to 2.60; P<0.001). The results for the original primary outcome of a modified Rankin scale score of 0 to 4 were 55% and 43%, respectively (adjusted rate ratio, 1.21; 95% CI, 0.95 to 1.54). Symptomatic intracranial hemorrhage occurred in 6 of 102 patients (6%) in the thrombectomy group and in 1 of 88 (1%) in the control group (risk ratio, 5.18; 95% CI, 0.64 to 42.18). Mortality at 90 days was 31% in the thrombectomy group and 42% in the control group (adjusted risk ratio, 0.75; 95% CI, 0.54 to 1.04). Procedural complications occurred in 11% of the patients who underwent thrombectomy.

CONCLUSIONS

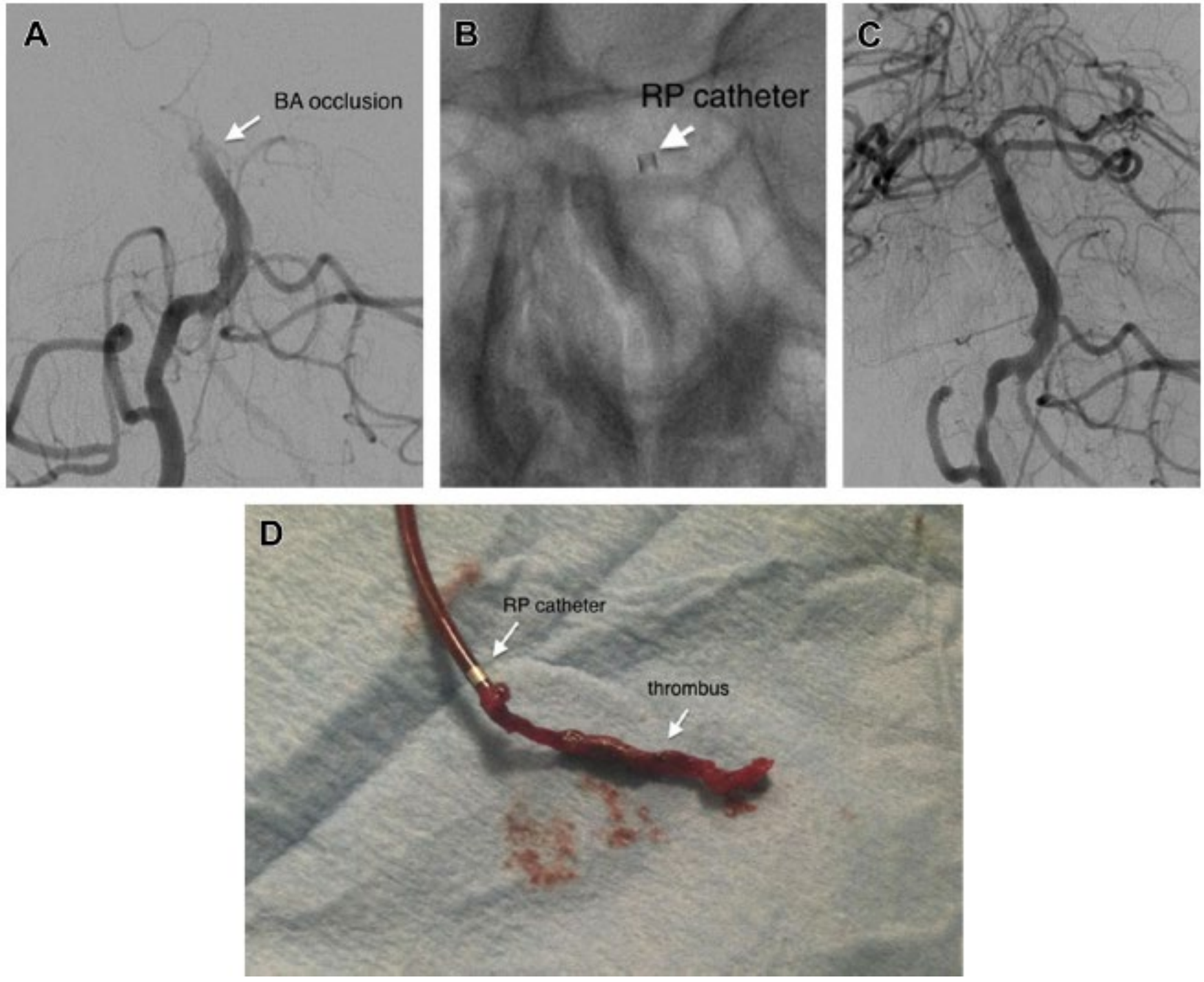
Among patients with stroke due to basilar-artery occlusion who presented 6 to 24 hours after symptom onset, thrombectomy led to a higher percentage with good functional status at 90 days than medical therapy but was associated with procedural complications and more cerebral hemorrhages. (Funded by the Chinese National Ministry of Science and Technology; BAOCHE ClinicalTrials.gov number, NCT02737189.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Ji can be contacted at jixm@ccmu.edu.cn or at the Department of Neurosurgery, Xuanwu Hospital of Capital Medical University, 45 Changchun St., Xi Cheng District, Beijing, 100053, China.

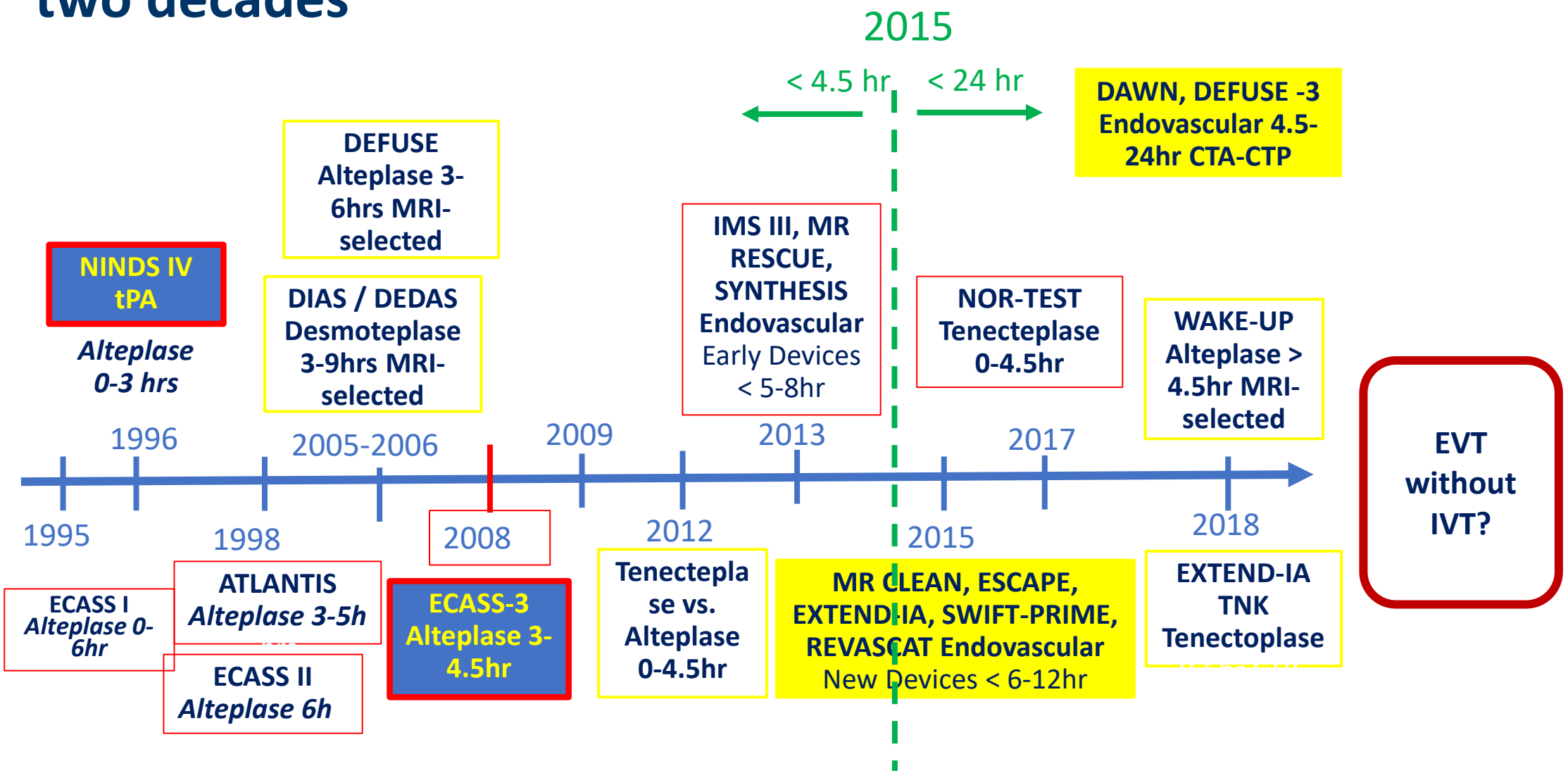
*A list of the BAOCHE investigators is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Jovin and C. Li contributed equally to this article.

N Engl J Med 2022;387:1373-84.
DOI: 10.1056/NEJMoa2207576


A
BA occlusion
B
RP catheter
C
D
RP catheter
thrombus

Evolution of Acute Ischemic Stroke (AIS) Care over two decades



Πρωτόκολλα ενδονοσοκομειακής αντιμετώπισης που εφαρμόζονται συνολικά από όλο το νοσοκομείο

Οργάνωση Αντιμετώπισης

Μονάδα Εγκεφαλικών Επεισοδίων

- A stroke unit
  - Is a dedicated and geographically defined part of a hospital that takes care of stroke patients
  - Has specialised staff with coordinated multidisciplinary expert approach to treatment and care
  - Comprises core disciplines: medical, nursing, physiotherapy, occupational therapy, speech and language therapy, social work [1]

ESO Guidelines 2008

Ολιστική φροντίδα

Θεραπείες επαναιμάτωσης

Μείωση αρτηριακής πίεσης

Θρομβοπροφύλαξη

Αποιδηματική αγωγή

Ν/Χ παρέμβαση

Έλεγχος πυρετού

Ρύθμιση γλυκόζης

Πρόληψη λοιμώξεων

National and Kapodistrian
UNIVERSITY OF ATHENS

Κέντρο Επεμβατικής Αντιμετώπισης Εγκεφαλικών

Συμπεράσματα

- Οι ασθενείς με οξύ ΑΕΕ πρέπει να υποβάλλονται άμεσα σε CT±CTA εγκεφάλου
- Επί απουσίας αντενδείξεων θρομβόλυσης θα πρέπει να λαμβάνουν ενδοφλέβια αλτεπλάση εντός 4.5 ωρών
- Σε ΑΕΕ της πρόσθιας κυκλοφορίας οι ασθενείς μπορούν να υποβληθούν σε θρομβεκτομή εντός 6 ωρών και επιλεγμένοι ασθενείς με βάση απεικονιστικά κριτήρια εως και 24 ώρες από την έναρξη των συμπτωμάτων
- Χρειάζονται περισσότερες μελέτες για τη θρομβόλυση με τενεκτεπλάση, τα ΑΕΕ της οπίσθιας κυκλοφορίας και το συνδυασμό θρομβεκτομής/θρομβόλυσης
- Οι θεραπείες επαναιμάτωσης στην οξεία φάση ελαττώνουν την αναπηρία και βελτιώνουν την ποιότητα ζωής
- Η αντιμετώπιση θα πρέπει να γίνεται με βάση οργανωμένα πρωτόκολλα, σε οργανωμένες μονάδες ΑΕΕ από κατάλληλα εκπαιδευμένο προσωπικό/διεπιστημονική ομάδα

Σας ευχαριστώ πολύ